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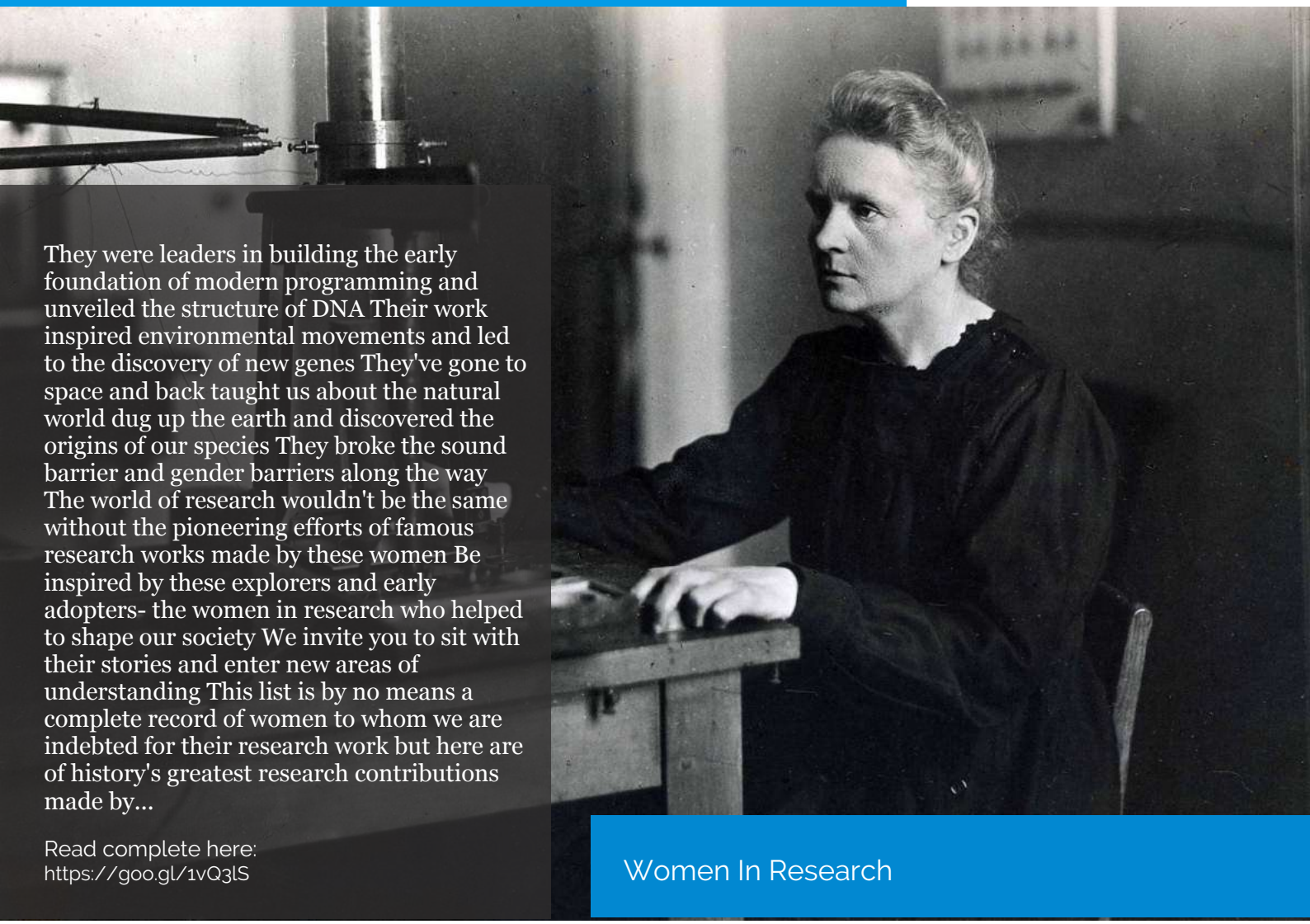

They were leaders in building the early foundation of modern programming and unveiled the structure of DNA Their work inspired environmental movements and led to the discovery of new genes They've gone to space and back taught us about the natural world dug up the earth and discovered the origins of our species They broke the sound barrier and gender barriers along the way The world of research wouldn't be the same without the pioneering efforts of famous research works made by these women Be inspired by these explorers and early adopters- the women in research who helped to shape our society We invite you to sit with their stories and enter new areas of understanding This list is by no means a complete record of women to whom we are indebted for their research work but here are of history's greatest research contributions made by...

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Treatment with Recombinant Enzymes Pbserum Medical High in a Patient Post Skin Grafts for Burns on the Right Lower Limb

Eugenia Paris & Jorge López-Berroa

ABSTRACT

Burns on the skin and their treatment have been considered a medical issue since ancient times. Approximately 90% of burns are of thermal origin, all of which involve tissue destruction. The depth and extent of the burn are important factors to consider when treating the injury.

Frequently, the resulting wounds are impossible to close or suture primarily, necessitating coverings such as grafts to achieve a stable and durable solution. However, these burns and their grafts can lead to pathological scars, which can have negative consequences for the individual, both aesthetically and physiologically, as they can impair proper movement of the affected limb. These scars are characterized by excess collagen deposition, making the use of the enzyme collagenase, which degrades this protein, relevant. Pbserum is a treatment line based on high molecular weight hyaluronic acid (HA) and a novel recombinant enzymatic system composed of collagenase, lipase, and liase. We present a case of a patient post skin grafts for burns on the right lower limb treated with High pbserum enzymes. This enzymatic cocktail proved to be safe and effective and resulted in the satisfactory evolution of the patient from the first application

Keywords: burns, hypertrophic scars, skin grafts, enzymes, collagenase, recombinant.

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Treatment with Recombinant Enzymes Pbserum Medical High in a Patient Post Skin Grafts for Burns on the Right Lower Limb

Eugenia Paris[α] & Jorge López-Berroa[σ]

ABSTRACT

Burns on the skin and their treatment have been considered a medical issue since ancient times. Approximately 90% of burns are of thermal origin, all of which involve tissue destruction. The depth and extent of the burn are important factors to consider when treating the injury.

Frequently, the resulting wounds are impossible to close or suture primarily, necessitating coverings such as grafts to achieve a stable and durable solution. However, these burns and their grafts can lead to pathological scars, which can have negative consequences for the individual, both aesthetically and physiologically, as they can impair proper movement of the affected limb. These scars are characterized by excess collagen deposition, making the use of the enzyme collagenase, which degrades this protein, relevant. Pbserum is a treatment line based on high molecular weight hyaluronic acid (HA) and a novel recombinant enzymatic system composed of collagenase, lipase, and liase. We present a case of a patient post skin grafts for burns on the right lower limb treated with High pbserum enzymes. This enzymatic cocktail proved to be safe and effective and resulted in the satisfactory evolution of the patient from the first application.

Its benefits were improvement in pigmentation and skin appearance, reduction of hypertrophic areas, and a more normal gait pattern, enabling a return to daily activities and significantly improving quality of life.

Keywords: burns, hypertrophic scars, skin grafts, enzymes, collagenase, recombinant.

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I. INTRODUCTION

Skin burns and their treatment have been considered a medical issue since ancient times. A burn results from the skin's contact with a heat source, which can be high temperatures, electricity, friction, radiation, and chemicals.

Burns can be classified according to other factors such as depth, etiology, and the percentage of body surface area affected. Regarding etiology, burn injuries can stem from thermal, electrical, chemical, and radiation contact, among others.

Around 90% of burns are typically of thermal origin, whether from hot liquids, dry heat via direct contact with flames or radiant heat, or contact with a hot object [1,2].

All burns involve tissue destruction due to energy transfer, associating different causes with different physiological and pathophysiological responses. Therefore, burn depth is an important factor to consider when treating the injury. Generally, the deeper the burn, the greater the demand for achieving good scar outcomes.

Following this criterion, a burn can be categorized as: (i) First-degree burns, which are superficial and only affect the epidermis; these burns are typically benign, very painful, heal without scarring, and do not require surgery. (ii) Second-degree burns, which affect the dermis and often form painful blisters; these burns range from superficial partial thickness (homogeneous, moist, hyperemic, and pale) to deep partial thickness (less sensitive, drier, may have a reticular pattern in erythema, and do not blanch).

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(iii) Third-degree burns, which are full-thickness. And (iv) fourth-degree burns, which require surgery, although they are generally nearly painless [2].

A long-term consequence of burns is scarring; these scars are flat and minimally discolored, characterized by increased collagenase activity, decreased expression of transforming growth factor beta (TGFβ), and macrophages with a predominant M1 phenotype. However, burns can lead to the development of pathological scarring [2]. Deep partial-thickness or full-thickness burns take longer to heal, resulting in a higher risk of pathological scarring, especially when combined with a prolonged acute inflammatory phase.

Pathological scars are characterized by excess collagen deposition, resulting in a thick, non-flexible layer that can cause itching, pain, and contractures, thus limiting functionality [2-3].

Two main subtypes of pathological scars are evident after thermal injury: hypertrophic scars and keloids. Hypertrophic scars are more common in burns and occur in 30-90% of patients. Conversely, keloid scars primarily occur in individuals with darker skin pigmentation and are raised fibroproliferative lesions composed of disorganized bundles of type I and type III collagen; moreover, they demonstrate un-controlled growth and invasion of normal tissues, along with a higher recurrence rate despite treatment [2-3].

Burn wounds often present as extensive avulsion of isolated skin and/or together with other tissues; thus, due to their significant extent and or involving deep dermis, they are impossible to close or suture primarily, necessitating alternative coverage methods to stabilize such wounds, such as grafts. Graft survival is feasible if the bed has sufficient granulation tissue, a good layer of subcutaneous cellular tissue, or if it involves muscle [4,5]. Nevertheless, grafts can also lead to pathological scars, with corresponding consequences. Therefore, it is important to anticipate or address such affected skin to prevent or mitigate its effects.

Regarding therapeutic management, scientific evidence suggests treatments such as intralesional corticosteroids, scar massage, intralesional 5-fluorouracil (for scars unresponsive to intralesional corticosteroids), bleomycin, pressure garments, pulsed dye laser, hyperbaric chamber, and radiotherapy [3]. Similarly, innovative formulations for wound healing have been implemented, including liposomes, nanoparticles [6], and enzymes. Enzymatic treatments have demonstrated benefits in dermatology and aesthetic medicine by increasing dermal permeability, enhancing blood flow and lymphatic drainage, reducing fibrous septae of cellulite, sagging, adiposity, and rejuvenating overall appearance; they also represent a minimally invasive aesthetic alternative [7]. Here we present our protocol for burns with High pbserum, a novel enzymatic treatment, in a patient with post-skin grafts.

II. CASE PRESENTATION

The patient is a 59-year-old woman who presented with a third-degree burn on the right lower limb, specifically in the tibial/fibular area, resulting from a gas cylinder explosion during a barbecue in August 2021. Initial treatment involved medical management of the burns with surgical debridement and various dressings. The patient required full-thickness skin grafts for the extensive lesion, which were performed three weeks after the day of the burn. The patient returned to the clinic three months after the grafts were performed, at which point a hypertrophic and hyperpigmented scar was evident (Fig. 1), along with hypersensitivity of the area, and inability to walk or wear a conventional shoe.

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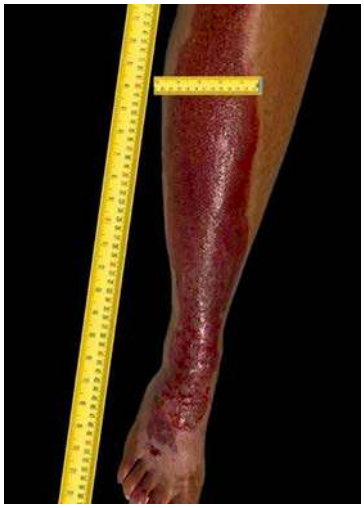

Figure 1: Skin condition 3 months post-grafts, December 2021

In 2017, the patient suffered a traffic accident resulting in monoplegia affecting the left lower limb; since then, she has been using a robotic device to walk and perform dorsiflexion of the left foot. Therefore, it is imperative to regain the range of motion of the limb with burn injury; additional treatment goals included improving the quality and appearance of the skin. Treatment was initiated six months after the skin grafts to ensure optimal adhesion to deep structures and achieve better treatment outcomes. Tissue retraction was considered to perform plantar grip of the foot, as the patient not only presented with tissue retraction but also fibrosis and hyperpigmented discoloration from the outset, which did not improve during the six months post-grafts.

The treatment of choice was High pbserum recombinant enzymes. This enzymatic cocktail consists of PB220 collagenase at a higher concentration, PB500 lipase, and PB72K liase. It is presented in a vial with lyophilized enzymes, a vial with 18 ml of reconstituting solution, and a sterile 5 ml syringe with 1.5 ml of high molecular weight HA [8]. Four enzyme kits were used for each application, totaling 80 ml of enzymatic dilution. Partial sedation with an anesthesiologist was used to reduce pain during treatment.

Injections were administered at a 15-30 degree angle to the skin. A total of 6 sessions were scheduled, spaced every six weeks. For optimal application of the enzymes at 1cc per cm2, the area was marked, completely delineating the outer edge of the grafts, and drawing a grid of squares with an area of $1cm^2$ across the entire extent of the graft. Enzyme application followed a predetermined order in an upward direction (Fig. 2).

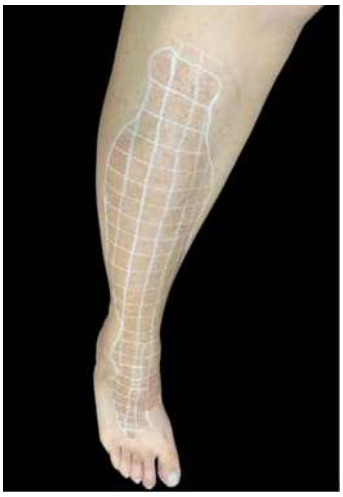

Figure 2: Marking for High pbserum treatment application

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At the time of the first enzyme application, good graft evolution was observed. The scar was hypertrophic, especially on the dorsum of the foot. The skin was rough to the touch and darkly pigmented, with very well-defined edges (Fig. 3A).

Marking was performed, followed by the application of 1.5 HA High pbserum enzymes. The result of the first session was a reduction in the hypertrophic area on the dorsum of the foot; a 1 cm decrease in the longitudinal edge of the lesion; an improvement in skin quality, smoother and softer to the touch; and changes in pigmentation.

The result of the second session was a further reduction in hypertrophy, along with continued improvements in pigmentation and lesion edges (Fig. 3B). After the third application, a marked decrease in pigmentation and hypertrophy was observed, along with changes in skin texture, increasing smoothness to the touch. Following the fourth session, the lesion exhibited a smaller diameter and length, with decreased pigmentation and reduced hypertrophy on the dorsum of the foot (Fig. 3C). The fifth session produced a notable change associated with complete reduction of fibrous tissue retraction on the dorsum of the foot, enabling the patient to perform full plantar flexion; changes continued regarding the length dimension of the scar and pigmentation; and hypersensitivity decreased, with the skin becoming smoother to the touch. At this point, the patient began walking again, going through all phases of gait, facilitating her daily activities. Two weeks after the sixth and final session, in February 2023, there was a reduction of over 70% in the edges of the lesion; complete reversal of hyperpigmentation, eliminating the dark coloration the patient had before enzyme application; the skin became even softer and more delicate; foot range of motion was fully restored, allowing for easy walking; and pain decreased significantly, enabling the patient to tolerate conventional footwear (Fig. 3D). The patient reported feeling happy and satisfied with the treatment outcome. As for side effects, at each application, the patient experienced marked edema, erythema, warmth, and 10 out of 10 pain on a scale of 10, for 72 hours. Additionally, she experienced difficulty walking and performing activities of daily living. No analgesics were used in this patient due to medical contraindications. Symptoms completely disappeared after seven days.

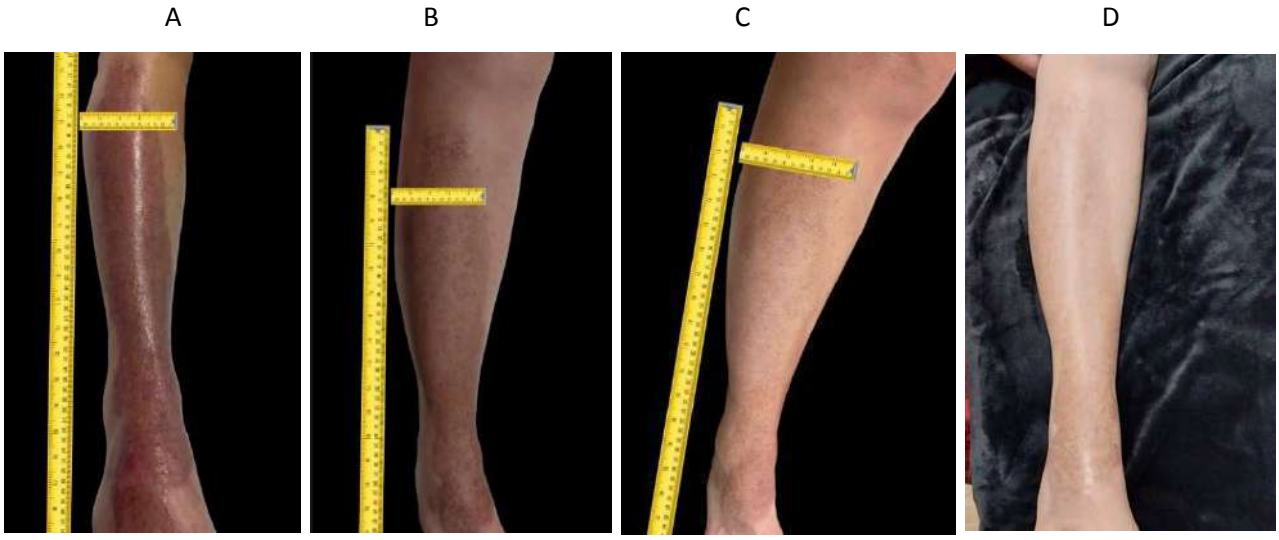

Figure 3: Evolution of pbserum treatment results. A) State of the right lower limb before the 1st application. B) Results after the 2nd application. C) Results after the 4th application. D) Two weeks after the 6th application

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III. DISCUSSION

Understanding the process of normal and pathological wound healing is essential for all medical and surgical specialties treating acute and chronic wounds, as the outcome of these processes will determine the final result of surgical treatment [3].

Our patient's scar, resulting from the third-degree thermal burn and subsequent grafting, was characterized by being hypertrophic, especially in the areas of the foot dorsum; hyperpigmented; extensive; rough and coarse; painful; and with skin retraction on the foot dorsum, impeding plantar flexion movement [2-3].

In hypertrophic scars, there is a proliferation of fibrotic connective tissue, leading to increased collagen synthesis and decreased degradation, resulting in an enhance in collagen type I fibers versus type III [8].

In the case presented here, we treated a hypertrophic scar with HA 1.5 High pbserum. We demonstrate how the combination of recombinant enzymes, collagenase, lipase, and liase, along with high molecular weight HA, improves skin appearance, eliminates hyperpigmentation, increases sensitivity, alleviates pain, and restores the patient's ability to walk easily by completely eliminating dorsum foot retraction. This enzymatic cocktail has a higher proportion of collagenase, which acts by breaking the peptide bonds of collagen, which is excessively deposited in pathological scars [2], and intervenes in its rearrangement, relaxing fibers with a smoothing and firming effect on the skin [7,9,10]. Additionally, the anti-inflammatory effect of high molecular weight HA alongside collagenase would help provide an optimal environment for skin recovery, resulting in increased hydration, reduced inflammation, and decreased fibrotic tissue; ultimately leading to a considerable improvement in our patient's skin area.

Previous results demonstrated how High pbserum decreased pruritus, pain, thickness, irregularities, and stiffness of hypertrophic, atrophic, and keloid scars from the first application [11]. However, this is the first case where the enzyme cocktail is applied to post-burn scars with grafts. Treatment commenced six months after grafting to ensure optimal adherence to the skin. The initial injections were administered, and upon observing positive changes, it was decided to continue applications every six weeks. The complete program consisted of six total sessions of short duration, providing a quick and comfortable practice where considerable improvement was evident in the patient with each session compared to the previous one.

In addition to the physiological and aesthetic changes observed, we obtained the patient's testimony regarding her satisfaction; the treatment enabled her to resume her daily activities and have a normal gait pattern, significantly improving her emotional state and quality of life.

The side effects observed were transient, lasting 72 hours, and disappeared to reveal the benefits of the treatment.

Burn injuries to the skin entail a greater demand to achieve good results in scar treatment. Therefore, science continues to advance in the development of novel techniques, and their application proves to be the choice of professionals in Aesthetic Medicine to ensure excellent results in their patients according to their needs. In our case, the results obtained with the cocktail of recombinant enzymes alongside high molecular weight HA 1.5 High pbserum align with one of the main purposes of Aesthetic Medicine: improving a person's appearance, providing greater well-being, and better overall health. Therefore, High pbserum could be considered an interesting alternative for post-burn patients, in terms of management, prevention, and rehabilitation, as many burns can lead to limitations in the range of motion of affected limbs.

IV. CONCLUSION

The benefits obtained following the application of 1.5 HA high pbserum in our patient with post-burn skin graft have been improvements in skin appearance (improve hyperpigmentation, smoothness, and firmness), reduction of

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hypertrophic areas, decrease in hypersensitivity, and restoration of movement; in addition to having a positive impact psychologically. Results were observed from the first application. Our protocol for pbserum enzyme application may serve as a safe and effective treatment alternative for burned patients with post-skin graft pathological scars. Further studies in this field are necessary to establish treatment recommendations.

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We want to express our sincere gratitude to the creators of second-generation enzymes for the benefits they have provided to patients. We wish to extend our gratitude to the patient for trusting our medical criteria. Likewise, we want to acknowledge and thank Dr. Valeria Kopytina for her continuous support and collaboration. And lastly, we thank Dr. Estefanía Hurtado Gómez for her great work in writing the article.

Conflict of Interest

Dra. Paris has no conflict of interest to declare. Dr. López Berroa is an employee of the company Proteos Biotech and he receives a salary for this purpose.

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An Approach to Knee Osteoarthrosis as a Significant Pathology in the General and Military Population

Nicolle Andrea Rodriguez Villaquiran, Maria Paula Duque Ceballos & Diego Alejandro Rodriguez Villaquirán

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ABSTRACT

Osteoarthrosis (OA) is one of the most common joint diseases. It affects a significant portion of the population, among which the military, who suffer mainly from post-traumatic knee osteoarthrosis. Being aware of this relationship fosters early preventive and/or protective behaviours among health personnel and allows them to proceed with timely therapeutic measures.

Keywords: osteoarthrosis, joint degeneration, mechanical disorders, military pathology.

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An Approach to Knee Osteoarthrosis as a Significant Pathology in the General and Military Population

**Abordaje De La Osteoartrosis De Rodilla Como Patología De Importancia En Población General Y Militar

Nicolle Andrea Rodriguez Villaquiran[α], Maria Paula Duque Ceballos[σ] & Diego Alejandro Rodriguez Villaquirán[ρ]

RESUMEN

La osteoartrosis (OA) es una de las enfermedades más comunes a nivel articular, se sabe que ésta posee una población significativa entre la cual la población militar también es afectada; relacionándose especialmente con la osteoartrosis de rodilla postraumática , Que se conozca dicha relación promueve de manera temprana conductas preventivas y/o protectoras por parte del personal de salud y una vez se identifique iniciar de manera oportuna medidas terapéuticas.

Palabras clave: osteoartrosis, degeneración articular, trastornos mecánicos, patología militar.

Objetivo Y Metodología: Orientar al profesional de la salud en el abordaje del paciente adulto con osteoartrosis de rodilla y resaltar la relación de dicha patología como una afeccion significativa en la población militar a través de una revisión de la literatura sobre el concepto básico de la enfermedad,su epidemiología , fisiopatología, los factores de riesgo a tener en cuenta y los múltiples abordajes terapéuticos a brindar.

Conclusión: El abordaje de la osteoartrosis de rodilla a través del entendimiento de la enfermedad y el reconocimiento de ésta como patología frecuente en la población general y aún más predominante en la población militar la cual tiene una mayor incidencia en trauma y un inicio más temprano de la enfermedad permitirá iniciar de manera oportuna medidas de prevención o el inicio de un tratamiento temprano que permita una atención asertiva.

ABSTRACT

Osteoarthrosis (OA) is one of the most common joint diseases. It affects a significant portion of the population, among which the military, who suffer mainly from post-traumatic knee osteoarthrosis. Being aware of this relationship fosters early preventive and/or protective behaviours among health personnel and allows them to proceed with timely therapeutic measures.

Keywords: osteoarthrosis, joint degeneration, mechanical disorders, military pathology.

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I. OBJECTIVE AND METHODOLOGY

To guide health professionals in the approach to the adult patient with knee osteoarthrosis and highlight the relationship of this pathology as a significant condition within the military population, by reviewing the literature on the basic concept of the disease, its epidemiology, pathophysiology, risk factors to be considered and the multiple therapeutic approaches to be provided.

II. CONCLUSION

The approach to knee osteoarthrosis through the understanding of the disease and the recognition of this as a frequent pathology in the general

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population, with a prevalence in the military, who have a greater incidence of trauma and an earlier onset of the disease, will allow timely preventive measures or early treatment to ensure assertive care.

III. INTRODUCCIÓN

La osteoartrosis (OA) es la más común de las enfermedades articulares y por lo tanto es una de las patologías con las que más se enfrentan en sus consultas todos los profesionales sanitarios , tanto especialistas como médicos de atención primaria (1,2)

Se define como un proceso degenerativo articular, consecuencia de trastornos mecánicos y biológicos que desestabilizan el equilibrio entre la síntesis y la degradación del cartílago articular (3). Además se es considerada como uno de los principales problemas de salud en todos los países (4).

Se describe que más del 50% de la población mayor de 65 años presenta algún tipo de OA, siendo la rodilla entre las más afectadas dado que carga la mayor parte del peso corporal y si bien se ha establecido una incidencia aproximada de 240/100.000 personas al año (5,6)

Se ha evidenciado que las tasas de OA fueron significativamente más altas en las poblaciones militares que en grupos de edad comparables en la población general. (7)

Los militares sufren de lesiones de todo tipo donde el trauma (el cual tiene una incidencia de lesiones de rodilla hasta 10 veces mayyor que el de la población general (8) es considerado una de las principales causas asociadas a lesiones de rodilla, aumentando de 3 a 6 veces la probabilidad de desarrollar OA. (9,10) también se les diagnostica aproximadamente 10 años antes que las personas sin antecedentes de traumatismo articular (8) y Dentro de los 5 años posteriores a la lesión, las rodillas presentan cambios estructurales que reflejan una salud articular alterada (p. ej., composición alterada del cartílago, estructura ósea alterada) (11 - 14). que refuerza el componente fisiopatológico.

IV. FISIOPATOLOGÍA

La etiología y desarrollo de esta patología no es entendido en su totalidad a día de hoy pese a la prevalencia tan elevada que presenta, pues solo se ha podido establecer algunos de los diversos factores, tanto mecánicos como químicos, que causan en combinación los cambios estructurales observables y los procesos fisiopatológicos que contribuyen a la progresión de la enfermedad. (15,16)

Previamente se consideraba que esta enfermedad presentaba un transcurso y desarrollo netamente mecánico, el cual se puede asociar a alteraciones del eje como rodillas varas o incluso lesiones traumáticas e inestabilidades multiligamentarias. (17) y Aunque la degradación del cartílago articular es lo primordial en la patogénesis, (18,19) Actualmente se ha establecido que es una enfermedad multifactorial asociado a distintas noxas que afectan el cartílago articular, membrana sinovial y hueso subcondral. (17,18,19) siendo el resultado final es una destrucción acelerada de la matriz por enzimas procedentes de los condrocitos y de las células sinoviales, seguida por alteraciones en los sistemas de reparación del cartílago (20).

La estructuración del cartílago articular se encuentra dividida en zonas denominadas como superficial o tangencial, intermedia o transicional y profunda o radial, las cuales son sometidas en presencia de esta patología al predominio del catabolismo frente a la síntesis de moléculas de matriz, además que asociado a la no vascularización de los cartílagos lo cual produce una limitación con respecto a los nutrientes y oxígeno aportados al mismo y a la baja capacidad regenerativa del cartílago, no hay realmente compensación con respecto al daño, dando la destrucción progresiva e irreversible de las mismas dando como desenlace la osteoartritis. (21.22)

La capa superficial se encuentra compuesta por células aplanadas, que permiten una mejor tolerancia a fuerzas de compresión, tensión y cizallamiento, y es donde se va a encontrar fibras colágenas finas, y un predominio de

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glicoproteínas pequeñas frente a las grandes. La capa media va a estar predominantemente conformada por células redondas las cuales se rodean de matriz extracelular y la capa profunda cuenta con un escaso recuento celular sin embargo cuenta con abundantes glucoproteínas.

Existe además un área calcificada o tidemark la cual se encuentra entre el cartílago y el hueso subcondral la cual es formada por la osificación endocondral, que tiene como función favorecer al factor mecánico de la articulación. (6,21)

Se ha descrito que durante el proceso patogénico se hace el daño de los tejidos por el catabolismo que se divide primeramente la fibrosis de la superficie articular y disminución de las glucoproteínas, lo cual al producirse el daño se genera un edema local y a su vez los fibroblastos presentes en la membrana sinovial generan un aumento de citoquinas y factores inflamatorios (IL-1, TNFa, TGF b, IL-8 y GROa) que causará junto al desgaste articular fisuras en el tejido fibroso que incluso pueden llegar a afectar el hueso directamente, y se culmina con la remodelación articular con la aparición y formación de quistes subcondrales, osteofitos, y se realiza un cambio del cartílago hialino por cartílago fibroso el cual tiene menor capacidad mecánica, a lo cual la progresión de la patología se puede dividir en 4 fases como se describen a continuación (16, 21).

- Fase 1: Actuación de los factores etiológicos.
- Fase 2: degradación de la matriz, inflamación y cambios reparativos.
- Fase 3: cambios en sinovial, cartílago y sinovia
- Fase 4: manifestaciones clínicas (dolor), impotencia funcional y destrucción articular

El estrés generado en la articulación es dado principalmente por un aumento de metaloproteinasas dependientes de zinc, como lo son la colagenasa mmp 1 y mmp 13, la estromelisina (mmp 3) y la agrecanasa, las cuales actúan directamente en el condrocito y se encargan de la degradación de matriz extracelular, glucosaminoglicanos, colágenos y proteínas. (21, 23)

Como se evidencia, en las fases iniciales de la patogénesis se ven alteraciones y cambios constitucionales de estructuras, más sin embargo no se presentan síntomas, pues realmente esta patología es indolora en estadios tempranos, ya que no es sino hasta la fase de remodelación de la articulación donde se realiza un proceso de angiogénesis con penetración en la capa profunda del cartílago articular que favorece asimismo la hipertrofia del hueso subcondral dando pie a los cambios anatómicos en la articulación, además de la aparición de fibras nerviosas de carácter sensorial que realmente son quienes se encargan de sensar los trastornos presentes y empiezan a aparecer las manifestaciones propiamente dichas (6, 23).

V. FACTORES DE RIESGO

Dependiendo de la articulación afectada, los factores son distintos, y se puede diferenciar entre una susceptibilidad generalizada donde encontramos factores de riesgo modificables y no modificables y factores locales de la articulación.

los cuales se describen más adelante y se resumen en la tabla 1. Con respecto a la población militar en múltiples estudios se ha evidenciado el aumento del riesgo de OA de rodilla con los siguientes factores; aumento de la edad, raza negra, rango militar mayor y personas que pertenecen específicamente a el ejército, fuerza aérea y la marina. (a)

6.1 Factores de Riesgo No Modificables

Edad: se considera que a mayor edad existe mayor probabilidad de pérdida de cartílago articular secundario a disfuncionalidad y al proceso degenerativo (24). Se describe que más del 70% de >50 años posee signos radiológicos de artrosis en alguna localización y prácticamente el 100 % a partir de los 75 años.

Factor Genético: se menciona que la heredabilidad de la OA de rodilla es del 40% (25) Sin embargo dado la diferencia de múltiples estudios se dificulta hacer predicciones precisas sobre la importancia de este componente (3) por lo que en otras literaturas se describe una baja asociación (6).

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Sexo: la artrosis se encuentra con mas prevalencia en el sexo femenino (3,4,5,6) y especificamente hablando de la rodilla en el compartimento femoropatelar en comparacion al hombre que se evidencia un mayor compromiso a nivel femorotibial (3).

Raza: frecuente en la población de raza blanca, pero las diferencias son poco relevantes.(3)

6.2 Factores de Riesgo Modificables

Sobrepeso/obesidad: Se ha sugerido un mecanismo mecánico, activando los condrocitos y acelerando la degeneración del cartílago con una especial susceptibilidad por parte de la articulación de la rodilla (3). Se encontró que el sobrepeso predispone a su desarrollo, la obesidad juega un papel importante en la disfuncionalidad articular y se determinó que el IMC es proporcional a padecer artrosis y discapacidad. (24).

Probablemente la causa principal sea el incremento de fuerzas mecánicas. Así, la mayor parte de obesos presenta deformidad en varo de las rodillas, lo cual incrementa las fuerzas que actúan en el compartimento femorotibial interno, acelerando el proceso degenerativo. (15).

Factores hormonales: El déficit estrogénico en la mujer está relacionado con el desarrollo de la artrosis, (3) Algunos estudios han demostrado que las mujeres que toman estrógenos tienen una prevalencia y una incidencia de OA menores que las que no los toman (26), sin embargo no ha sido concluyente su relación (3)

Densidad Mineral Ósea: no está claro que exista una relación inversa entre la aparición y el desarrollo de la artrosis y la densidad mineral ósea (3,26)

6.3 Factores de Riesgo Locales

Anomalías articulares: congénitas, displasias, defectos de alineación, traumatismos, laxitud articular y la Sobrecarga articular por ejercicio físico de alta intensidad y el deporte de alta competición pueden acelerar el desarrollo de la artrosis a causa del sobreuso y los traumatismos de repetición (3) En cuanto al trauma específicamente, se ha visto que la rodilla suele ser una de las articulaciones más afectadas, la incidencia puede ser para lesiones meniscales en personas activas físicamente de 0.33 a 0.61 por 1000 persona/año y en población militar activa el mismo tipo de lesión alcanza la alarmante cifra de 8.27 por 1000, este tipo de lesiones han demostrado un aumento en el riesgo de desarrollar osteoartritis de rodilla (27).

Tabla 1: Factores de Riesgo Osteoartrosis

Factores de riesgo generales NO modificables	Factores de riesgo locales
Edad Genética Sexo Raza	• Anomalías articulares previas • Inestabilidad articular / • hipermovilidad. • Forma articular anormal (congénita o adquirida). • Traumatismos y fracturas • Malformaciones o displasia • Defectos de alineación • Inestabilidad y laxitud articular • Meniscopatías • Artropatías neuropáticas • Sobrecarga articular (actividad física y laboral)
Factores de riesgo generales modificables	
Sobrepeso/Obesidad Factores hormonales Densidad mineral ósea	

Fuente: Elaboración propia. (3, 4, 5, 6, 15, 20, 24, 25)

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VII. DIAGNÓSTICO

El diagnóstico de esta patología debe realizarse de manera temprana para intervenir la sintomatología y trata de impactar en la progresión, la principal herramienta diagnóstica es la clínica del paciente, se debe investigar entonces por historia familiar, factores de riesgo y posibles desencadenantes, aquí cobra vital importancia en población militar indagar específicamente por actividad física y laboral (por ejemplo movimientos repetitivos de la articulación), historia de lesiones traumáticas previas como lesiones meniscales, ligamentarias, entre otras, que nos permitan sospechar la patología. Se debe caracterizar el dolor para diferenciar un componente mecánico de uno inflamatorio con preguntas como localización, intensidad, frecuencia, duración, dolor con el reposo o con el movimiento, desencadenantes del dolor y mejoría con uso de analgesicos o cambio de actividad. (28)

En cuanto a la exploración física de manera general es importante tomar el peso e IMC del paciente, se debe evaluar la marcha buscando inestabilidad, deformidades o limitación, con el movimiento buscar crepitaciones, dolor o limitación en arcos de movimiento, al palpar buscar aumento del volumen articular y finalmente valorar la fuerza de la extremidad. (28).

VIII. AYUDAS DIAGNÓSTICAS

Radiografía: la radiografía sigue siendo una herramienta de bajo costo y el método estándar para realizar el diagnóstico en la mayoría de los pacientes, se ha evidenciado en militares con historia de lesiones traumáticas en rodilla un aumento en la prevalencia de cambios radiográficos sugestivos de oa comparado con otros sin historia de lesión traumática (29). En este tipo de imagen se pueden apreciar la degeneración del cartílago y los cambios esqueléticos (30). Para asegurar una buena calidad técnica se requieren tomar las siguientes proyecciones; anteroposterior, lateral, axial de rótula y de Rosenberg, en esta última se aprecia mejor la disminución del grosor del cartílago (31).

Una vez se cuenta con la imagen y según los hallazgos se procede a clasificar en 5 grados según lo descrito por Kellgren-Lawrence y el cual se puede apreciar en la tabla 2.

Tabla 2: Características radiológicas OA. Adaptado de (32)

Grado	Características Rx
0	Sin alteraciones. Normal
1 (OA dudosa)	Estrechamiento indeterminado del espacio articular. Posible presencia de osteofitos
2 (OA leve)	Posible estrechamiento del espacio articular. Presencia de osteofitos
3 (OA moderada)	Estrechamiento evidente del espacio articular. Presencia de múltiples osteofitos, de manera moderada. Esclerosis leve. Posible deformidad de la epífisis.
4 (OA grave)	Estrechamiento marcado del espacio articular. Abundantes osteofitos Esclerosis grave Deformidad epifisaria confirmada

Resonancia magnética: este estudio permite evaluar las características del cartílago, estructuras blandas periarticulares y descartar diagnósticos diferenciales como necrosis (31), la mayoría de pacientes mayores de 40 presentan cambios degenerativos en este estudio por lo cual debe realizarse un buen análisis y considerar este tipo de ayuda diagnóstica en casos puntuales

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como pacientes que continúan con síntomas y radiografía normal, cuando se requiere un cambio en el manejo o que tengan adicionalmente patologías inflamatorias (28).

IX. TRATAMIENTO

El tratamiento de los pacientes con osteoartrosis debe ser un tratamiento integral, multidisciplinario y sistémico a largo plazo, teniendo en cuenta las características de la población militar, teniendo en cuenta el estadio clínico del paciente, los factores de riesgo que posee y el grado de afectación funcional. Debe incluir además de los medicamentos, cambios en el estilo de vida que permitan impactar sobre los factores de riesgo modificables y brindar finalmente calidad de vida y disminución del deterioro articular de esta población a largo plazo.

De manera general el tratamiento se apoya de medicamentos y medidas de rehabilitación y soporte que tienen como pilares la reducción y el control de síntomas, conservar la flexibilidad articular y aumentar la calidad de vida, entre ellas se encuentra el control de peso, prescripción adecuada de ejercicio, uso de antiinflamatorios y analgesicos, ortesis, terapia fisica, entre otras (33).

9.1 Medidas no farmacológicas

Pérdida de peso: una de las medidas fundamentales es la pérdida de peso, como se describió anteriormente un gran porcentaje del peso corporal, está distribuido en la articulación de la rodilla (34). Se recomienda en este tipo de pacientes un índice de masa corporal menor de 25. En las metas terapéuticas se debe dialogar con el paciente que cualquier pérdida de peso es benéfica, pero entre más alto el porcentaje de pérdida, mayor es el beneficio terapéutico y debe ir en conjunto con el programa de ejercicio y terapia física (35, 36)

Ejercicio y rehabilitación: Controla dolor y mejora funcionalidad, esta herramienta se usa como uno de los pilares de tratamiento en población militar (37), mediante ejercicios terapéuticos, estos buscan disminuir el pico mecánico de la carga focal del cartílago por impacto, genera efecto de bombeo del líquido sinovial para nutrir el cartílago y estimula al tejido conectivo. Debe ser supervisado y modificable, de baja a mediana intensidad inicialmente para evitar un ejercicio mal estructurado que podría por el contrario empeorar la condición del paciente al generar microtraumatismos.

El programa de ejercicio debe incluir un componente aeróbico, de flexibilidad (el cual genera menor impacto positivo) y de fortalecimiento muscular algunos ejemplos de esto son; caminata de 30 minutos seguidos en terreno llano con calzado cómodo, ejercicios acuáticos y bicicleta estática que absorbe el impacto. Estiramiento muscular de miembro inferior con énfasis en cuádriceps e isquiotibiales y para fortalecimiento de tipo isométrico e isotónico con contracción muscular con peso inmovil y aumento gradual de la fuerza.

Adicional al ejercicio se debe incluir terapia manual y educación en la enfermedad. En caso de que el ejercicio aumente la limitación funcional, se debe remitir el paciente a fisioterapia, además de que es primordial explicar a los pacientes que en las etapas iniciales el dolor puede aumentar de manera transitoria (34, 35, 36).

Ortesis: Se ha descrito el uso de cintas o vendajes para disminución del dolor, además del uso de bastones para mejorar la deambulación, según un consenso de medicina física y rehabilitación, no se recomienda usar braces en pacientes sintomáticos, además de que el uso del bastón puede impactar en analgesia pero con riesgo de sobrecargar otras articulaciones. No recomendar de manera rutinaria a menos de que el paciente posea inestabilidad de la articulación o carga biomecánica anormal (35,36)

9.2 Medidas farmacológicas

De los medicamentos disponibles para el tratamiento de la osteoartrosis se encuentra el grupo de los analgesicos que reduce el dolor pero no impacta en la progresión de la enfermedad, los antiinflamatorios que dan analgesia con mayor potencia, pero tienen efectos adversos que limitan su uso a largo plazo y los modificadores

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que disminuyen la progresión. Entre las vías de administración podemos encontrar fármacos tópicos, orales, intramusculares, intravenosos e intra articulares (38)

Acetaminofen: fármaco de primera línea para el manejo del dolor en osteoartrosis en múltiples guías de manejo, a pesar de la evidencia de bajo beneficio e incluso fallo terapéutico como monoterapia y como terapia a largo plazo. Es un fármaco seguro y económico que se usa para dolor de intensidad leve a moderada, tiene un menor efecto analgesico comparado con los AINE y se debe considerar su potencial efecto hepatotoxicidad como efecto adverso, se recomienda su uso con una dosis máxima de 3g día en dosis divididas (39)

Antiinflamatorios no esteroideos: influyen en el metabolismo de citoquinas en líquido sinovial, con alivio satisfactorio del dolor, el diclofenaco y el ibuprofeno disminuyen la interleucina 6, factor de necrosis tumoral alfa en el líquido sinovial de la articulación afectada con mejoría en la funcionalidad, tienen un mayor efecto analgesico por lo cual algunas guias en los últimos años los posicionan como primer opcion terapeutica, numerosos estudios sostienen su eficacia a corto plazo, se pueden utilizar como rescates, en ciclos cortos de uso, limitados en tiempo por sus potenciales efectos adversos entre ellos los gastrointestinales, se recomienda usarlos en la menor dosis posible (40)

Los AINE tópicos son fuertemente recomendados por el colegio americano de reumatología por menor exposición sistémica al medicamento y reducción del dolor, entre ellos el ketoprofeno y el diclofenaco tópico han demostrado buenos niveles de reducción del dolor en pacientes con osteoartrosis (39, 41)

Opioides: fármacos que brindan analgesia con mecanismo de acción central, adecuados en dolor moderado a severo, que no logran control analgesico con farmacos de menor potencia analgesica y medidas no farmacológicas, se recomienda iniciar con opioides débiles entre los cuales encontramos tramadol, codeina, dihidrocodeina y opioides fuertes con menor evidencia cuando el dolor es crónico y no logra respuesta con las opciones anteriores entre los cuales encontramos oxicodona, hidromorfona, morfina y en parches como fentanilo y buprenorfina. Idealmente considerar los opioides débiles por ciclos cortos de uso, en monoterapia o en compañía de fármacos de menor potencia, además de valorar de manera continua su perfil de seguridad y posibles efectos adversos como el estreñimiento, náuseas, emesis, sedación, prescribiendo de manera concomitante fármacos que controlen estos efectos secundarios (42).

9.3 Intraarticulares

Antiinflamatorios esteroideos: en su forma de inyectables intraarticulares, tienen un potencial efecto benéfico en manejo del dolor, especialmente en pacientes con signos inflamatorios y de derrame articular, duración del efecto de dos a diez semanas, no hay diferencia entre corticosteroides. Se deben considerar cuando no hay respuesta a otros tratamientos farmacológicos y/o para soportar la terapia física (35,36,43)

Ácido hialurónico: la pérdida de viscoelasticidad del líquido sinovial en la osteoartrosis, se puede considerar como uno de los mecanismos causantes del dolor y la disminución de la movilidad en la articulación, se ha considerado la viscosuplementación como una de las posibles terapias, entre estas soluciones de ácido hialurónico que aportan alta viscoelasticidad a la articulación, inyecciones semanales con solución Hylan GF20 han probado ser seguras y eficaces con analgesia de hasta 6 meses. En guías como la del colegio americano de reumatología dan recomendación cautelosa y dejan esta terapia como decisión conjunta con el paciente, dado su evidencia y beneficio limitado, pero como una potencial opción cuando otras alternativas terapéuticas han fallado (38,39)

9.4 Tratamiento quirúrgico

La respuesta al tratamiento no quirúrgico suele tener resultados estáticos y no alentadores en algunos casos, cuando la osteoartrosis se encuentra en estadios severos o falla terapéutica a múltiples tratamientos, las intervenciones

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quirúrgicas como las prótesis totales o parciales, artrodesis, artroscopias entre otros se convierten en una solución para los pacientes, su meta es la reducción del dolor, disminuir la discapacidad y mejorar la calidad de vida, siempre considerando las comorbilidades únicas y expectativas con el tratamiento de cada paciente
(44, 45).

Los proveedores que tratan lesiones agudas en la población militar deben comprender cuál es la mejor manera de minimizar el impacto de las lesiones articulares de alta energía en términos de riesgo futuro de PTOA.(46)

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Does the Implementation of a Children's Story Improve a Child's Hospital Stay?

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SUMMARY

Introduction: The admission of a child to a health institution, on some occasions, is due to the performance of a procedure such as surgery. Parents and the child express doubts, anxiety and even, on some occasions, forget to comply with a pre-surgical requirement. To improve this situation, the idea arose to implement a story that tells the story of a child and his family so that, in this way, they can know what will happen to them and, thus, reduce anxiety. In addition, they are given a checklist, so that they do not forget important actions and materials prior to surgery.

Objectives: To implement, in the pre-surgical stage, an educational children's story for parents and the child to read before their intervention, in order to reduce anxiety during their hospital stay.

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Does the Implementation of a Children's Story Improve a Child's Hospital Stay?

¿La Implementación De Un Cuento Infantil Mejora La Estadía Hospitalaria De Un Niño?

Prof. Mg. Lorena Cecilia Gonzalez

RESUMEN

Introducción: El ingreso de un/a niño/a a una institución de sanidad, en algunas ocasiones, se debe a la realización de un procedimiento como una cirugía. Los padres y el niño manifiestan dudas, angustia e inclusive, en algunas ocasiones, se olvidan de cumplir con algún requisito prequirúrgico. Para mejorar esta situación, surgió la idea de implementar un cuento que narre la historia de un niño y su familia para que, de esta manera, puedan conocer lo que le sucederá y, así, reducir la ansiedad. Además, se les da una lista de chequeo, para que no se olviden de acciones y materiales importantes previos a la cirugía.

Objetivos: Implementar, en la etapa prequirúrgica, un cuento infantil educativo para que los padres y el niño lo lean antes de su intervención, a fin de reducir la ansiedad durante su estadía hospitalaria.

Material y métodos: Se realiza un estudio cualitativo y descriptivo a través de una encuesta sobre la opinión a profesionales de la salud que atienden a niños. Esta es sobre la implementación de un cuento que narre en forma escrita y con imágenes la estadía del niño en el hospital. Es un momento que los padres y el niño pueden compartir, para hablar sobre la estadía hospitalaria. El acceso a la encuesta es voluntario.

Resultados: Se encuestó al 100% del personal (N.º 19), de los cuales un 31,5% (N.º 6) son psicólogos; el 10, 5% (N.º 2), psicopedagogos; el 10, 5% (N.º 2), licenciados en Enfermería; el 31,5% (N.º 6), especialistas en Enfermería en Cuidados Intensivos Pediátricos; el 15,8% (N.º 3), especialistas en Enfermería Neonatal, que trabajan en una Unidad de Cuidados Intensivos Pediátricos. El 89,4% pertenece al género femenino (N.º 17) y el 10,5%, al masculino (N.º 2). Al 100% le pareció apropiada la implementación del cuento.

Sobre el tema de que el cuento evite los malentendidos, un 84,2% (N.º 16) respondió que SÍ. Un 5,3% respondió que el cuento no iba a evitar la solución de errores. Y, en la variable "Otras", un 10,5% (N.º 2) describió que iba a servir para calmar al niño, dependiendo de lo adaptado que estuviera el cuento para la edad del niño y para su capacidad de comprensión.

Conclusiones: Esta herramienta surge de la realización de un cuento educativo más una lista de chequeo con el fin de evacuar dudas que no se pueden tal vez despejar en la consulta, ya que es escueta por el shock emocional y por la etapa de duelo. Por esta razón es importante conocer la opinión de profesionales que están en contacto y acompañan a los niños y a la familia en la estadía hospitalaria. El 100% implementa esta herramienta educativa.

Palabras clave: consulta médica en pediatría, cuento infantil educativo, rol de la enfermería.

SUMMARY

Introduction: The admission of a child to a health institution, on some occasions, is due to the performance of a procedure such as surgery. Parents and the child express doubts, anxiety and even, on some occasions, forget to comply with a pre-surgical requirement. To improve this situation, the idea arose to implement a story that tells the story of a child and his family so that, in this way, they can know what will happen to them and, thus, reduce anxiety. In addition, they are given a checklist, so that they

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do not forget important actions and materials prior to surgery.

Objectives: To implement, in the pre-surgical stage, an educational children's story for parents and the child to read before their intervention, in order to reduce anxiety during their hospital stay.

Material and methods: A qualitative and descriptive study is carried out through an opinion survey of health professionals who care for children. This is about the implementation of a story that narrates in written form and with images the child's stay in the hospital. It is a time that parents and child can share to talk about the hospital stay. Access to the survey is voluntary.

Results: 100% of the staff (No. 19) were surveyed, of which 31.5% (No. 6) are psychologists; 10.5% (No. 2), educational psychologists; 10.5% (No. 2), graduates in Nursing; 31.5% (No. 6), specialists in Pediatric Intensive Care Nursing; 15,8% (No. 3), specialists in Neonatal Nursing, who work in a Pediatric Intensive Care Unit. 89.4% belong to the female gender (No. 17) and 10.5% to the male gender (No. 2). 100% thought the implementation of the story was appropriate.

On the topic of the story avoiding misunderstandings, 84.2% (No. 16) responded YES. 5.3% responded that the story was not going to avoid solving errors. And, in the "Other" variable, 10.5% (No. 2) described that it would serve to calm the child, depending on how adapted the story was for the child's age and ability to understand.

Conclusions: This tool arises from the completion of an educational story plus a checklist in order to clear up doubts that may not be able to be cleared up in the consultation, since it is brief due to the emotional shock and the stage of mourning. For this reason, it is important to know the opinion of professionals who are in contact with and accompany children and the family during their hospital stay. 100% implement this educational tool.

RESUMO

Introdução: A internação de uma criança em uma instituição de saúde, em algumas ocasiões, uma cirurgia. Os pais e a criança expressam dúvidas, ansiedade e até, em algumas ocasiões, esquece de cumprir uma exigência pré-cirúrgica. Para melhorar esta situação, surgiu a ideia de implementar uma história que conte a história de uma criança e da sua família para que, desta forma, possam saber o que lhes vai acontecer e, assim, reduzir a ansiedade. Além disso, eles recebem um checklist, para que não se esqueçam de ações e materiais importantes antes da cirurgia.

Objetivos: Implementar, na fase pré-cirúrgica, uma história infantil educativa para os pais e a criança lerem antes da sua intervenção, de forma a reduzir a ansiedade durante o internamento hospitalar.

Material e métodos: Estudo qualitativo e descritivo realizado por meio de pesquisa de opinião com profissionais de saúde que atendem crianças. Trata-se da implementação de uma história que narra de forma escrita e com imagens a permanência da criança no hospital. É um momento que pais e filhos podem compartilhar para conversar sobre a internação. O acesso à pesquisa é voluntário.

Resultados: Foram pesquisados 100% dos funcionários (nº 19), dos quais 31,5% (nº 6) são psicólogos; 10,5% (nº 2), psicólogos educacionais; 10,5% (nº 2), graduados em Enfermagem; 31,5% (nº 6), especialistas em Enfermagem Intensiva Pediátrica; 15,8% (nº 3), especialistas em Enfermagem Neonatal, que atuam em Unidade de Terapia Intensiva Pediátrica. 89,4% pertencem ao género feminino (nº 17) e 10,5% ao género masculino (nº 2). 100% acharam que a implementação da história foi apropriada.

Sobre o tema da história evitando mal-entendidos, 84,2% (nº 16) responderam SIM. 5,3% responderam que a história não evitaria a resolução de erros. E, na variável "Outros", 10,5% (nº 2) descreveram que serviria para acalmar a criança, dependendo do quão adaptada a história fosse para a idade e capacidade de compreensão da criança.

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Conclusões: Essa ferramenta surge a partir do preenchimento de uma história educativa crescida de um checklist para esclarecer dúvidas que talvez não consigam ser esclarecidas na consulta, por ser breve devido ao choque emocional e à fase do luto. Por este motivo, é importante conhecer a opinião dos profissionais que contactam e acompanham as crianças e a família durante o seu internamento hospitalar. 100% implementam esta ferramenta educacional.

I. INTRODUCCIÓN

En la actualidad, el sistema de salud debe satisfacer las demandas de sus pacientes, haciendo que el sistema de turnos se adecue a las necesidades de ellos y a lo que la institución necesita para mantenerse en el mercado. En este punto, la calidad en la prestación del servicio se define según la conformidad; múltiples funciones técnicas, científicas administrativas; recursos humanos, económicos; relaciones interpersonales; y la perspectiva del paciente que fundamenta si dichas acciones llegaron a satisfacer sus necesidades y expectativas por el servicio brindado[1].

¿Pero cuánto es el tiempo necesario para garantizar la calidad en el entendimiento sobre su estado de salud, describir las alternativas de tratamiento de manera sencilla para que todos los involucrados lo comprendan, y tomen una decisión? En ese encuentro, el especialista debe darles todas las indicaciones sobre la preparación, cuidados previos al procedimiento, a fin de disipar muchos temores y dudas por el shock de dicha noticia. Todos los seres humanos tienen distintas formas de responder según su experiencia, su cultura, su religión, su formación y sus características particulares.

En Buenos Aires, el promedio en tiempo de esta consulta es de quince minutos en clínica médica; puede ser algo mayor en algunas especialidades como pediatría o como salud mental. Esto se ve reflejado en el programa de honorarios que tenga la clínica u hospital: si cobra honorario por cada consulta o si es un salario mensual. Lo aconsejable, según una encuesta que realizó la Sociedad Argentina de Cardiología (cuyos resultados demostraron que al 70% de los profesionales se le exige ofrecer turnos de 10 a 15 min cuando, en realidad, para ellos, lo recomendable es que sea de entre 20 y 30 min[2]). En este artículo haremos hincapié en la atención del paciente pediátrico y sus padres, teniendo en cuenta que, con solo una consulta médica, no se logra la promoción de la salud.

La enfermedad de un niño es un hecho innovador frente a su rutina: sucede una crisis, comienza a sufrir y a pensar cómo puede afectar esto en el futuro, dependiendo de la edad que tenga. Es importante centrarse en dos pilares: el educativo, y el psicológico/afectivo. En este caso, los padres interpretan la información que reciben acerca de la enfermedad, su etiología, sus síntomas, su curso y su tratamiento[3]. Debido a la brevedad del tiempo de la consulta, los padres pueden encontrarse abrumados. Por ello, en ese momento de la consulta, se puede entregar un cuento infantil donde se describirá el proceso que atravesarán el/la niño/a y su familia durante su estadía en el hospital.

El cuento infantil es una herramienta didáctica, que actúa como facilitadora de pensamiento desde una experiencia pedagógica, la imaginación y la creatividad. Posibilita respuestas para el/a niño/a de acuerdo a la experiencia pedagógica realizada.

[1] Vargas González, Vilma; Valecillos, José; Hernández, Carmen Calidad en la prestación de servicios de salud: Parámetros de medición Revista de Ciencias Sociales (Ve), vol. XIX, núm. 4, octubre-diciembre, 2013, pp. 663-671 Universidad del Zulia Maracaibo, Venezuela. https://www.redalyc.org/articulo.oa?id=28029474005

[2] DELIA OUTOMURO1, ANDREA MARIEL ACTIS. Estimación del tiempo de consulta ambulatoria en clínica médica. Rev Med Chile, 2013; 141: 361-366).

[3] Quesada Conde, Ana Belén; Justicia Díaz, M. Dolores; Romero López, Miriam; García Berbén, M. Trinidad LA ENFERMEDAD CRÓNICA INFANTIL. REPERCUSI- ONES EMOCIONALES EN EL PACIENTE Y EN LA FAMILIA. International Journal of Developmental and Educational Psychology, vol. 4, núm. 1, 2014, pp. 569-576 Asociación Nacional de Psicología Evolutiva y Educativa de la Infancia, Adolescencia y Mayores Badajoz, España. Disponible en: https://www.redalyc. org/pdf/3498/349851787062.pdf

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Los cuentos infantiles que facilitan un aprendizaje armónico e incluyen la participación de la familia, permitieron comprender cómo los mensajes de un cuento terminan consolidando el andamiaje del proceso de aprendizaje[4].

Se realiza un cuestionario a licenciados en Enfermería y a especialistas que trabajan en el servicio de cuidados críticos pediátricos. A continuación, se detallan reacciones de pacientes que no recibieron instrumentos o información sobre su internación:

- Algunos retienen al hijo como si el profesional le fuera a realizar un daño.
- Otros lloran desconsoladamente delante del paciente.
- Verbalizan: "¿Ya se van?", haciendo referencia a los agentes de salud.
- Otros verbalizan: "Dicen que el/la enfermero/a es malo/a". Estos comentarios son negativos para la evolución del niño. Los niños absorben todo y pueden temer por ellos, ya que el/la enfermero/a va a compartir muchos momentos con el niño y con su familia.
- Muchos padres no les informan a sus hijos lo que les va a suceder. Les dicen que van a hacerles un estudio (cuando, en realidad, el paciente es intervenido quirúrgicamente) y regresan a su casa. Luego, cuando es intervenido quirúrgicamente, el niño pierde confiabilidad respecto de los padres y se muestran enojados.

En el momento en que visitan al especialista (en este caso, vamos a hablar de un cirujano cardiólogo), se fija la fecha de procedimiento, y se les da a los padres, en forma oral, todas las indicaciones y algunas escritas. Pero esos papás (por ejemplo, si el niño llora en la consulta o por el momento mismo que atraviesan) no tienen la capacidad de memorizar, y luego pueden cometer errores, ya que en algunos casos muchos padres no realizaron los baños prequirúrgicos; no suspendieron drogas de anticoagulación; no respetaron el ayuno; no llevaron el consentimiento para la cirugía. Todos estos motivos harán que se demore dicho procedimiento y que deba reprogramarse la fecha. También pueden incurrir en errores que pueden ser aún más graves si no se detectan.

Para su contención, es importante reducir la ansiedad brindando conocimientos sobre lo que pasará en su estadía de internación. Si surgen dudas, pueden anotarlas y consultar a un operador, mediante un número telefónico que se le brinda para tal fin.

El personal de Enfermería tratará, mediante comunicaciones directas con el paciente, padre/madre o tutor del niño, y hará lo siguiente manera durante la internación:

- Asesorar sobre el procedimiento a realizar, sin detallar los procedimientos médicos, dado que estos son competencia del personal médico, y una información inexacta podría generar falsas expectativas en el paciente y en su familia.
- Brindar normas de la institución, horario de visitas e, inclusive, de visita de los padres.
- Notificar las horas aproximadas que durará la cirugía, según lo que informe el cirujano.
- Hacerles conocer los cuidados prequirúrgicos y posquirúrgicos.
- Brindarles la oportunidad de participación del cuidado y tratamiento, siempre y cuando no interfiera en el bienestar del paciente.
- Informar sobre la trayectoria del lugar y sobre la experiencia del equipo tratante acerca de la grave problemática que atraviesa su hijo/a.
- Mostrarles la sala de espera, hall, o habitación de cada institución, donde puedan ser ubicados sin inconvenientes.
- Tomar sus datos, número telefónico o la ubicación del lugar donde esperarán que finalice el procedimiento.
- Preguntar si tienen alguna duda y recomendarles que anoten sus dudas para poder obtener respuestas en el momento del parte médico.

[4] Jiménez Ortíz, Martha Lucía; Gordo Contreras, Aurora El cuento infantil: Facilitador de pensamiento desde una experiencia pedagógica Praxis & Saber, vol. 5, núm. 10, julio-diciembre, 2014, pp. 151-170 Universidad Pedagógica y Tecnológica de Colombia .png, Colombia. Disponible en: https://www.redalyc.org/articulo.oa?id=477247214009.

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- No brindar un parte con diagnóstico médico, pero sí contarles sobre los signos y síntomas que pueda llegar a tener su hijo/a y cuáles van a ser los procedimientos de enfermería.

Es necesario que la familia esté informada sobre lo que sucederá en su estadía; de esta forma, el niño será protagonista, y todo será más natural. Por este motivo se nos ocurrió la escritura de un cuento en el cual el protagonista es el niño que va a ser sometido a un procedimiento, y se le cuenta todo lo que vivirá en su estadía. El cuento se le entregará a la familia luego de la consulta del especialista. ¿Por qué?

La toma de decisión de un tratamiento (el cual es un procedimiento invasivo) es un momento muy abrumador para los padres. Dependiendo de su edad, el niño nota los cambios en el estado anímico de sus padres, lo cual repercute en su estado en el momento de la internación. Muchas veces intentan prestar atención, pero luego no recuerdan, dudan, lo que genera más estrés en ellos. El cuento, al finalizar, presenta un lista de chequeo para que los padres verifiquen todas las actividades que deben realizar.

II. OBJETIVOS

Implementar en la etapa prequirúrgica un cuento infantil educativo para que los padres y el niño lo lean antes de su intervención, a fin de colaborar en su estadía en la internación.

III. MATERIAL Y MÉTODO

Se realizó un estudio descriptivo cualitativo con el fin de explorar las opiniones de acuerdo a sus conocimientos de agentes de salud que trabajan con paciente pediátricos y con padres. Entre ellos se encuentran psicólogos, psicopedagogos, licenciados en Enfermería, especialistas en Enfermería Neonatal, para conocer sus puntos de vista con la realidad cotidiana de la internación de los niños y su evolución en la internación, con la implementación de un cuento educativo, donde se relatará lo que sucederá en su estadía (este se detalla más adelante). Los profesionales que participaron fueron a través de una encuesta con preguntas cerradas y abiertas. Su accesibilidad fue de manera voluntaria.

¿Por qué la elección de este instrumento? El cuento infantil es una serie simple y lineal con escenarios descritos muy brevemente, cuyos personajes están brevemente caracterizados y realizan acciones muy claras para el/la niño/a, con un final adecuado a la sucesión de los hechos. Algunas funciones que debe cumplir un cuento infantil que refleje la vida diaria e imaginaria colaboran para calmar una determinada situación[5].

A continuación, se mostrará un cuento escrito y diseñado con la finalidad de que los padres lo lean y luego le comenten a su hijo/a a través de los dibujos de tal manera que el niño comprenda lo que sucederá. De esta manera los tres tendrán conocimiento de qué se trata la estadía en el hospital. A continuación les presentaremos el cuento de un niño que tiene un problema cardiovascular y cuyos padres deben prepararlo para la cirugía. Luego del cuento, hay una lista denominada *check list*, que sirve para que los padres revisen las acciones que deben realizar y lo que deben llevar ese día.

[5] Molina Cantabella, Gloria Esther. Cuentoterapia, el cuento como recurso educativo en la etapa de infantil. PublicacionesDidacticas.com; 2017; Número 81, Pág 194-198.

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SALVADOR

Había una vez un niño de cuatro años de edad, que se llamaba *Salvador*. Vivía con su mamá y con su papá en una casa en el centro de la ciudad de Buenos Aires. Sus papás lo veían decaído, un tanto más cansado que lo habitual. La mamá de Salvador era docente; al comentarle a una maestra lo que le pasaba a su hijo, esta le aconsejó que lo llevara al pediatra.

Sus padres, entonces, pidieron una consulta al pediatra para saber qué le estaba pasando a su hijo y si necesitaba algún tratamiento médico. El día de la consulta era el 13 de enero.

Ese día, Salvador estaba muy asustado porque él no recordaba de qué se trataba ir al consultorio de un pediatra, ya que la última vez que había ido era más pequeño. Pero sí recordó que ese día había visto unos dibujitos de los personajes que le gustaban mucho, lo cual eso le dio cierta tranquilidad: no había peligro.

En ese momento, entendió que el médico lo iba a ayudar a que se sintiera mejor y a recuperar las ganas de jugar como antes.

Llegaron al consultorio. El pediatra saludó a Salvador con un puñito, y le dijo: "No tengas miedo; te cuento cómo va a ser la visita de hoy. Primero, les voy a hacer unas preguntas a tus papás y después te voy a escuchar con esto: es un estetoscopio; no duele. Te voy a revisar, te voy a escuchar el corazón y los pulmones, y luego te voy a pedir, por ejemplo, que respires profundo.

Luego, el pediatra redactó unas órdenes para completar algunos estudios necesarios para arribar al diagnóstico.

Los tres salieron del consultorio, luego de haber saludado al médico, quien le regaló un chupetín al niño.

SALVADOR

Pasaron algunos días. Salvador fue al hospital a hacerse una ecografía. El médico le explicó de qué se trataba el estudio. Le dijo: "No tengas miedo: este es un estudio muy simple, que no te va a provocar ningún tipo de dolor. ¿Ves este equipo? Vamos a ver en la pantalla tu corazón, a escuchar tus latidos: 'Tun, tun'. También vamos a poder ver cómo se mueve ese corazondito".

Salva tuvo curiosidad y se levantó la remera como un superhéroe.

Pidió:

—¿A ver?

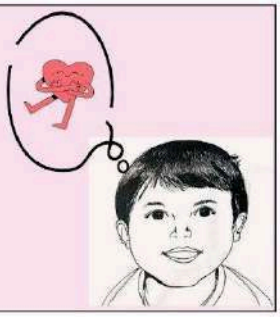
—Salva, ¿escuchás? Ahora mirá; te muestro: ¿ves que acá —señaló el monitor— se mezcla la sangre de color azul y roja? Tu corazón tiene un pequeño agujerito, que hay que curar. ¡Así tu corazón va a estar más Fuerte!

Una vez que terminó la visita, los tres saludaron al médico.

Durante los días siguientes, continuaron el circuito para completar los estudios solicitados por el pediatra.

Una enfermera le realizó un electrocardiograma. Le contó previamente en qué consistía y le explicó que, para que el dibujito saliera bien, era necesario que se quedara quieto. Le colocó unas pinzas en sus tobillos y en sus muñecas, y le puso unos chupetes de goma en el pecho. Le aclaró que esos chupetes podrían causarle algunas cosquillitas, pero que no eran molestos. Además, le explicó que ese estudio era necesario porque mostraba la intensidad de los latidos de su corazón a través de algunos dibujos.

Luego de haber finalizado el estudio, los recibió el médico cardiólogo. Salvador le preguntó a su mamá qué hacía un cardiólogo. La mamá le respondió: "El cardiólogo es un especialista que se encarga de ver tu corazón y de estudiarlo para poder curarlo".



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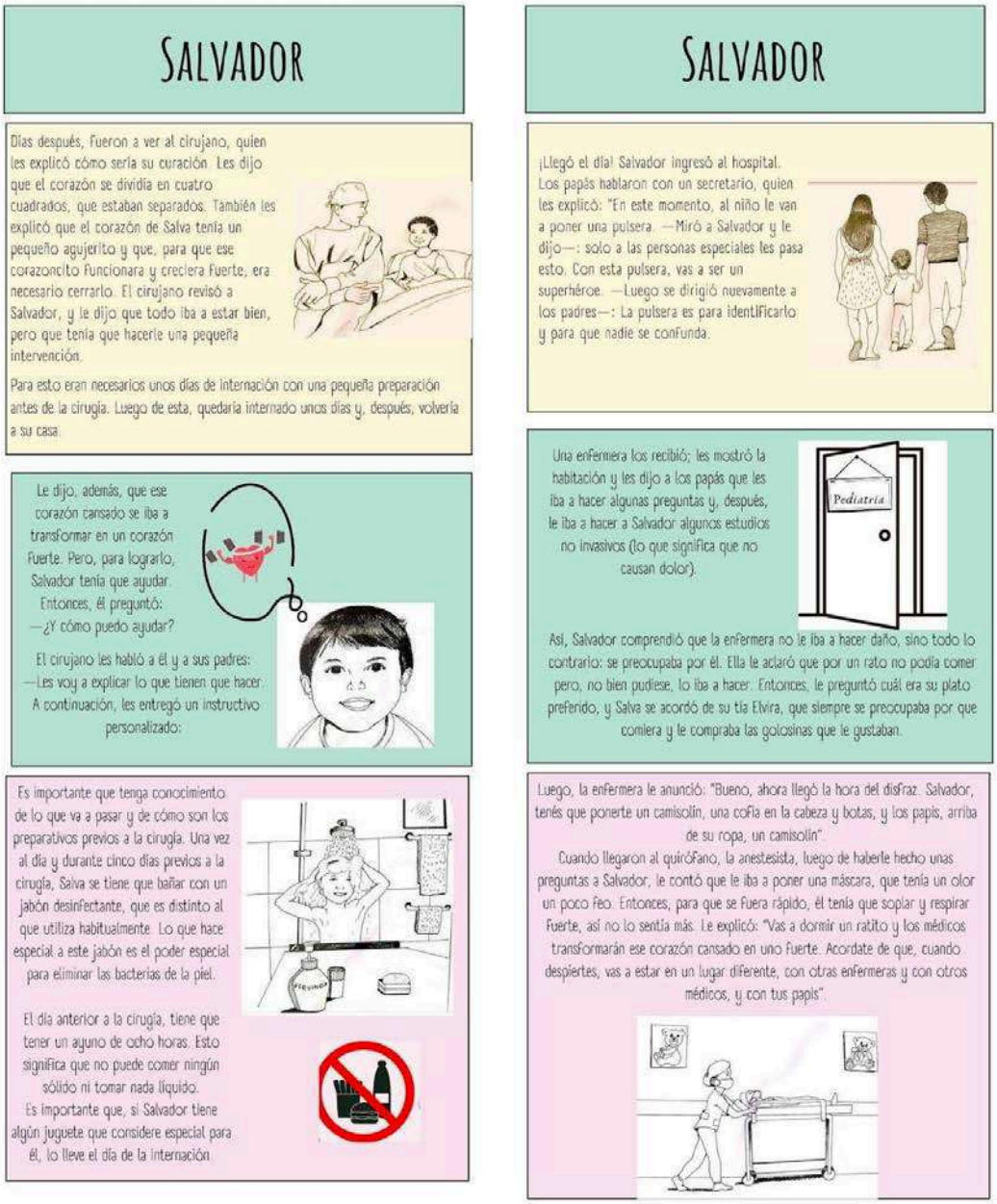

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Antes de su internación (la cual es conjunta: pueden ir ambos padres con el niño), deben recordar:

Actividades	Sí
Baños con antiséptico (clorhexidina jabonosa) durante los 5 días previos a la fecha de cirugía.	
Traer el muñeco u objeto de transición favorito del niño.	
Traer todos los estudios realizados.	
Calendario de vacunas completo.	
Ayuno de líquidos y de sólidos (consultar el tiempo de ayuno con el médico).	
Tener la parte administrativa resuelta.	
Consentimiento informado.	
Recordar los fármacos para tomar durante el tratamiento.	
Recordar suspender fármacos según indicación médica.	
Informar si es alérgico a un fármaco y/o producto.	
Informar si el paciente sufre (o sufrió) de convulsiones.	
Si tiene dudas, puede llamar al … (detallar el número que corresponda).	
Chequear, en el momento de la internación, que la pulsera identificadora tenga la información correcta.	
Dejar su número telefónico.	
Ropa interior del niño, vestimenta holgada y calzado cómodo del niño.	
Recordarle al médico de guardia la comida que le gusta al niño (para después de la cirugía).	
Si el niño recibe lactancia materna y usted tiene extractor, recuerde traerlo.	

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Comentarle a la enfermera cuál es el nombre del niño y cómo lo llaman.	
Contar a los agentes de salud qué música lo relaja y qué dibujos animados le gustan.	
Si deciden ir a descansar porque el niño está durmiendo, se le entregará un teléfono, por el cual estarán comunicados.	
Informar si el niño tuvo vómitos, diarrea, fiebre dentro de las 48 h previas.	

IV. RESULTADOS

Se encuestó al 100% (N.° 19), del cual un 31, 5% (N.° 6) eran psicólogos; el 10,5 % (N.° 2), psicopedagogos; el 10, 5% (N.° 2), licenciados en Enfermería; el 31, 5% (N.° 6), especialistas en Enfermería en Cuidados Intensivos Pediátricos; el 15, 8% (N.° 3), especialistas en Enfermería Neonatal, que trabajan en una Unidad de Cuidados Intensivos Pediátricos. El 89, 4% (N.° 17) pertenecía al género femenino y el resto, el 10, 6% (N.° 2), al masculino.

Al 100% le pareció apropiada la implementación del cuento. Se les consultó qué puntaje le darían, considerando el 1 como muy mala implementación y 10, como muy buena.

Las respuestas fueron las siguientes:

Un 63,2% (N.° 12) respondió: “10”.

Un 5,3% (N.°1) respondió: “9”.

Un 10,6% (N.° 2) respondió: “8”.

Un 21% (N.° 4) respondió: “7”.

Otra de las preguntas se refirió a si este cuento puede solucionar el tema de errores, de malentendidos en la preparación del niño que será sometido a una cirugía. Un 83,3% (N.° 15) respondió que SÍ. Un 5,5% respondió que el cuento no iba a evitar la solución de errores. Y, en la variable “Otras”, un 11% (N.° 2) describió lo siguiente:

- Va a servir para calmar al niño.
- Depende de lo adaptado que esté el cuento para la edad del niño y para su capacidad de comprensión.

V. COMENTARIOS LIBRES

- Creo que es una propuesta interesante, ya que puede servir a que el niño, mediante los personajes del cuento, pueda identificar de forma mediatizada situaciones de angustia para poder verbalizarlas, involucrándose imaginariamente en la problemática en la que se encuentra inmerso.

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- La información previa acerca de lo que se le va a hacer o lo que va a pasar puede reducir los efectos de ansiedad, estrés, bajar la incertidumbre, etc.
- Me parece fundamental que el niño y la familia cuenten con herramientas y personal que ayuden a mejorar su salud de manera integral. Pienso que, durante la internación, también es muy importante que la institución cuente con una sala de juegos terapéutica en el lugar.
- Me resulta importante la psicoeducación a la hora de una internación en una unidad pediátrica, y más en casos donde hay procesos invasivos.
- Es una buena herramienta y recurso para niños y para padres, a fin de acompañar ese proceso de internación.
- Las cirugías y todo lo relacionado con el ámbito médico suele generar miedo y cuestionamientos en los niños, por lo cual me parece muy interesante y útil poder abordar una cirugía mediante un cuento.
- Creo que resulta de suma importancia acercar material didáctico a los/as niños/as, así como a las familias sobre el proceso de internación al que se verán sometidos. El uso de una herramienta artística como lo es el cuento permitirá poner en palabras los pensamientos, emociones y miedos a los que el grupo familiar (y particularmente los/as niños/as) se verán expuestos. Por otra parte, ofrecer información real y concreta permite disminuir las fantasías (muchas veces ansiógenas) sobre la realidad del tratamiento que se llevará a cabo, y una mirada más realista y certera de lo que sucederá.
- Me parece superdidáctico e innovador, ya que es una situación difícil tanto para padres como para los niños. Hacerlo de esta forma más lúdica es enriquecedor.
- La implementación de un cuento sería una manera de llegar a los niños y poder explicarles lo que sucederá durante su internación, ya que muchas veces no llegan a entender qué es lo que sucede, y tienen miedo.
- Las consultas médicas son muy cortas para evacuar y contener al paciente y su familia. La situación es abrumadora, y algunos padres quedan en shock por someter a su hijo a una cirugía, el miedo, la duda de si hicieron lo correcto. Cuando llegan a la internación, muchos se muestran aterrados y transmiten ese malestar al niño, lo cual hace caótica la estadía (primero, por ellos y luego por las intervenciones que hay que realizar, las cuales, por falta de información y por miedo del pacientito, no se pueden realizar). Conclusión: es una agonía para todos….
- Debería ser más corto o más largo dependiendo de la edad de cada niño/a o del tipo de procedimiento, con pictogramas para niños con discapacidad en el neurodesarrollo o braille para quienes no puedan ver.
- El cuento debe estar enfocado en lo que se va a realizar.
- Es muy original la idea. Apoyo la iniciativa.
- Me parece una idea apropiada para la atención de los niños y de la familia.
- Me parece una implementación muy buena; tengamos en cuenta que, la mayoría de las veces, la enfermería no cuenta con el personal adecuado, pero me encanta. ¡Éxitos!
- Es necesario anticipar al niño lo que va a suceder, y un cuento me parece un método que podría ser efectivo.
- Creo que implementar información en forma de cuentos no solo ayudaría al niño a adquirir información más fácil de entender, sino también a las personas adultas que los acompañan, ya que muchas veces es mucha información técnica/ médica que tiene que procesar.
- Considero que es una herramienta que puede ser valiosa.

VI. CONCLUSIONES

Es importante tomar consciencia sobre la reducción en el tiempo de las consultas médicas, la cual no llega a satisfacer las demandas emocionales, educativas, adquisición de habilidades, y dudas por parte de los padres y de los niños. Además, no existe una enseñanza de cómo deben comportarse los padres para que la estadía sea más llevadera. Sabiendo que es un estado muy angustiante (y más cuando se trata de una cirugía de alta complejidad), surge la necesidad de crear un cuento para padres y niños

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que transitan esa etapa, y conocer la opinión profesional de agentes de salud que son muy importantes en esta etapa. El cuento debe ser adecuado para cada institución. Al 100% de los encuestados le parece adecuada su implementación.

AGRADECIMIENTOS

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Royal Family's Cancer Diagnoses Offer a Supreme Authority to Rectify Cancer Therapies to Save Cancer Patients

Ming C. Liau, Christine L. Craig & Linda L. Baker

ABSTRACT

The recent cancer diagnoses of King Charles and Princess Kate, while a misfortune no one wishes to happen, offer a supreme authority to rectify cancer therapies to save cancer patients. Cancer incidence and mortality continue to increase during the past 50 years. Obviously, cancer has not been eradicated.

The health profession is an authoritarian profession. When the establishments at the very top of health professions make a mistake, there is no way to rectify the mistake, and the mistake carries on to hurt patients. It will depend on higher authorities to rectify the mistake. King Charles and Princess Kate are in such positions to force changes of current cancer therapies to save themselves and other cancer patients, many of them are in a hopeless situation created by the current therapies.

Keywords: cancer therapy, chemotherapy, differentiation therapy, immunotherapy, CDA, CSCs, DIs, DHIs, PSCs, Wound healing.

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Royal Family's Cancer Diagnoses Offer a Supreme Authority to Rectify Cancer Therapies to Save Cancer Patients

Ming C. Liau[α], Christine L. Craig[σ] & Linda L. Baker[ρ]

ABSTRACT

The recent cancer diagnoses of King Charles and Princess Kate, while a misfortune no one wishes to happen, offer a supreme authority to rectify cancer therapies to save cancer patients. Cancer incidence and mortality continue to increase during the past 50 years. Obviously, cancer has not been eradicated. The health profession is an authoritarian profession. When the establishments at the very top of health professions make a mistake, there is no way to rectify the mistake, and the mistake carries on to hurt patients. It will depend on higher authorities to rectify the mistake. King Charles and Princess Kate are in such positions to force changes of current cancer therapies to save themselves and other cancer patients, many of them are in a hopeless situation created by the current therapies.

Cancer therapy has had a bad start by relying on toxic chemicals to kill cancer cells (CCs) and the disappearance of tumor as a criterion for the judgment of therapeutic efficacy. These were mistakes made by cancer establishments at a time when we did not have the complete understanding of cancer. Now we have better knowledge of cancer, but the cancer establishments are still trapped in the failed principle of killing of CCs and the disappearance of tumor to direct cancer therapies. Cancer evolves as a consequence of wound unhealing due to the collapse of chemo-surveillance. Wound healing requires the proliferation and the terminal differentiation of progenitor stem cells (PSCs). Chemo-surveillance is the nature's creation of allosteric regulation on abnormal methylation enzymes (MEs) to achieve terminal differentiation. Abnormal MEs are also the nature's creation to allow the buildup of PSCs to heal the wound. MEs of PSCs are abnormal due to association with telomerase. The buildup of PSCs is limited by contact inhibition. The nature does not create a mechanism to rectify the breakdown of chemo-surveillance. Inability to complete terminal differentiation of PSCs forces PSCs to evolve into cancer stem cells (CSCs) in order to escape contact inhibition. By a single hit to silence TET-1 enzyme, which is well within the reach of PSCs equipped with abnormally active MEs, PSCs can be easily turned to become CSCs.

The proliferation of CSCs still cannot heal the wound, because the problem is the breakdown of chemo-surveillance. CSCs are then forced to progress to faster growing CCs by chromosomal abnormalities such as translocations to activate oncogenes or deletions to inactivate suppressor genes. Evidently, cancer evolves due to wound unhealing. Therefore, the appropriate solution of cancer is to follow the wound healing process.

Pro-wound healing is the right approach of cancer therapy. Cancer establishments pursue the opposite approach by treating with toxic chemicals or agents that create more wounds to aggravate the already bad situation to result in horrendous cancer fatalities. Cancer establishments are responsible for the failure of cancer therapies. King Charles and Princess Kate are the supreme authorities to direct the right approach of cancer therapies to save themselves and other cancer patients in the same situation.

We have carried out extensive studies of natural and unnatural differentiation inducers (DIs) and differentiation helper inducers (DHIs) for the manufacturing of cell differentiation agent (CDA) formulations to save cancer patients. The development of CDA formulations was constantly blocked by cancer establishments,

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We have carried out extensive studies of natural and unnatural differentiation inducers (DIs) and differentiation helper inducers (DHIs) for the manufacturing of cell differentiation agent because CDA formulations ran against their wish on the claim of tumor shrinkage as a criterion of effective cancer drugs. Recent success of immunotherapy of cancer appears to support the cancer establishments' stance on cell killing as the commanding principle of cancer therapy. It is undeniable that immuno-surveillance plays an important role to prevent cancer evolution.

Chemo-surveillance and immuno-surveillance are both protection mechanisms created by the nature to ward off cancer, one against wounds created by toxic chemicals and the other against wounds created by infectious agents. Both protection mechanisms can be synergistic to eliminate cancer causing factors. But these two protection mechanisms can also be antagonistic to each other. Cachexia symptoms are triggered by immunological reactions, which is responsible for the collapse of chemo-surveillance. In this sense, immunological approach is harmful to cancer therapy. Immunotherapy is definitely a better version of cytotoxic cancer therapy than chemotherapy. But the outcome is the same to cause increasing cancer mortality, because immunotherapy is unable to solve the problem of CSCs. CDA formulations are the only viable solution of CSCs, and the solution of cancer depends on the solution of CSCs.

Keywords: cancer therapy, chemotherapy, differentiation therapy, immunotherapy, CDA, CSCs, DIs, DHIs, PSCs, Wound healing.

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I. INTRODUCTION

Cardiovascular diseases are the number one cause of death. Cancer is the second leading cause of death worldwide. Health profession is hapless to solve these two giant killers. Cardiovascular diseases may be difficult to overcome. Cancer is actually a simple matter, but is not handled right by the cancer establishments. Cancer can be solved if cancer establishments can be replcaed [1]. When leading health establishments continue to practice ineffective therapies, there is no mechanism to rectify the decision to continue with current ineffective therapies. This mistake is continuing to hurt patients. It will depend on authoritative figures higher than the current establishments to initiate change. The recent cancer diagnoses of King Charles and princess Kate, while unfortunate, could potentially bring attention to current practices to rectify cancer therapies to save themselves and other cancer patients. Many patients are in hopeless situation created by the current cancer therapies still used by top cancer establishments [2]. Cytotoxic drugs create damages to trigger the proliferation of CSCs to work on the repair of damages they created. In most primary cancer, the proportion of CSCs is usually less than 2% of the tumor mass.

CSCs are protected by drug resistance and anti-apoptosis mechanisms. They are not responsive to cytotoxic drugs or radiation. The proportion of CSCs will increase to reach a high level no longer responsive to further treatment. Primary brain cancer has a very high level of CSCs above 10% [3, 4], which is not responsive to cytotoxic cancer therapy. The ineffectiveness of cytotoxic drugs against CSCs and the contribution to the damage of chemo-surveillance are the reason for the horrendous cancer mortality caused by cytotoxic drugs and radiation.

According to NCI experts, the cancer incidence was 19 million and the cancer mortality was 10 million in 2019 worldwide, which were a 5% increment from the previous year [5]. They predicted a 5% yearly increment likewise in the following years. Drugs are developed to save patients, however, cytotoxic drugs contribute horrendous cancer fatalities, which must be eliminated to save cancer patients [6].

II. COMMENTARIES AND DISCUSSION

II.1 Abnormal MEs as the Most Critical Issue of Cancer

Cancer is basically a problem of growth regulation going awry. MEs are at the center of growth

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regulation playing a pivotal role on the regulation of cell replication and differentiation, therefore these enzymes are critically involved with cancer.

MEs are a ternary enzyme complex consisting of methionine adenosyltransferase (MAT)- methyl-transferase (MT) - S-adenosylhomocysteine hydrolase (SAHH) [7]. In steroid hormone targeted organs, SAHH is the steroid hormone receptor.

SAHH requires steroid hormone to assume a stable configuration to form a dimeric complex with MT, which has a molecular size similar to MAT. MT-SAHH and MAT then form a ternary enzyme complex, which is the stable and active unit. Steroid hormone functions as an allosteric regulator to promote MEs to active ternary enzyme complex. Without steroid hormone, ternary enzyme complex dissociates to become inactive individual enzymes. MTs in the monomeric form have a tendency to be modified to become nucleases that can cause damages to result in cell apoptosis. MEs most important for the regulation of cell replication and differentiation are 2'O-ribose MEs of pre-rRNA which control the production of ribosome [8, 9] and DNA MEs which control the expression of tissue specific genes [10]. Because of the important regulatory role on cell growth, MEs are subjected to exceptional allosteric regulation [11].

In telomerase expressing cells, MEs are associated with telomerase [12]. The association with telomerase changes kinetic properties of MAT-SAHH isozyme pair, and the regulation greatly in favor of cell growth. K_m values of telomerase associated MAT-SAHH isozyme pair are 7-fold higher than those of normal isozyme pair [7, 12, 13]. The higher K_m is an indication that MEs of telomerase expression cells are much more stable than normal MEs, since Prudova et al. found S-denosylmethionine (AdoMet) could protect protein against protease digestion [14].

Larger pool sizes of AdoMet and S-adenosylmohocysteine (AdoHcy) are evidently important for the maintenance of cell growth of cells expressing telomerase, since Chiba et al. found greatly shrunk pool sizes of AdoMet and AdoHcy when HL-60 cells were induced to undergo terminal differentiation [15]. Apparently, abnormal MEs play a critical role on the buildup of cells expressing telomerase, such cells include CSCs, CCs, embryonic stem cells (ESCs) and PSCs.

Evidently, the buildup of ESCs and PSCs is a normal process in the development of fetus and in the process of wound healing. Abnormal MEs do not cause problems in the execution of such normal processes. On the contrary, if the buildup of stem cells is prematurely interrupted by speeding up terminal differentiation, e.g. by the administration of thalidomide, normal development will be affected, resulting in malformation of body parts notably limbs. The nature creates safety mechanisms such as contact inhibition, TET-1 enzyme to direct lineage transitions and chemo-surveillance to prevent unwanted buildup of stem cells with abnormal MEs. Only when such safety mechanisms become dysfunctional or damaged, cells with abnormal MEs evolve to become CSCs and CCs to create clinical symptoms.

PSCs are ESCs to initiate the development of specific organs or tissues. A small fraction, usually less than 2% of the organ or tissue mass is reserved for the future expansion or repair, which requires the proliferation and the terminal differentiation of PSCs [16]. On wound healing, wound triggers biological and immunological responses. The biological response involves the release of arachidonic acid (AA) from membrane bound phosphatidylinositol through phospho-lipase A2 for the synthesis of prostaglandins (PGs) by cyclooxygenases and PG synthases [17, 18].

Although AA and PGs are active DIs [19], which are chemicals capable of eliminating telomerase from abnormal MEs, the induction of terminal differentiation of PSCs at the initial stage of wound is not the primary objective of PGs.

Rather, the localized inflammation caused by PGs [20] is responsible for the increase of membrane permeability to facilitate the extravasation of plasma proteins and regulatory factors into the wound resulting in edema response, which is the primary objective of PGs to orchestrate the

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healing process. Chemo-surveillance mediated through DIs and DHIs, which are inhibitors of MEs capable of potentiating the activity of DIs, normally functions as a brake to prevent the buildup of PSCs. This brake must be released in order for PSCs to proliferate to produce enough cells to heal the wound. PGs are metabolically unstable [17]. Their biological effects are most likely brief and confined to the wound area. Thus, the promotion of the proliferation of PSCs is the primary objective of PGs on wound healing, whereas the induction of terminal differentiation of PSCs at the final stage of wound healing is accomplished by DIs and DHIs of chemo-surveillance. The stable end products of PGs, namely dicycloPGs, are also active as DIs, although not as active as PGs [19], which may get involved in the promotion of terminal differentia tion of PSCs at the final stage of wound healing. Destabilization of abnormal MEs through chemo-surveillance is the critical mechanism of wound healing, which dictates the success of wound healing as well as cancer therapy [21, 22]. Consequently, restoration of chemo-surveillance, which is destroyed in order for cancer to show up [23], is a top priority of cancer therapy [24]. The biological response of the wound producing PGs is good for wound healing. The immunological response producing cytokines is not good for wound healing. Tumor necrosis factor (TNF) among cytokines produced is particularly bad for wound healing [25, 26]. On one hand, it causes the apoptosis of stem cells to trigger proliferation of PSCs, and, on the other hand, it causes cachexia symptoms to result in the collapse of chemo-surveillance. The collapse of chemo-surveillance removes the brake to promote the proliferation of PSCs. The expansion of normal stem cells is limited by contact inhibition.

If wound cannot be healed due to the collapse of chemo-surveillance, which the nature does not have a mechanism to rectify, PSCs will be forced to evolve into CSCs in order to escape contact inhibition. It takes a single hit to silence TET-1 enzyme to turn PSCs to become CSCs [27, 28], which is within the reach of PSCs equipped with abnormally active MEs. The propagation of CSCs still cannot heal the wound, because the problem is the collapse of chemo-surveillance. The slow replicating CSCs will be forced to progress to faster growing CCs by chromosomal abnormalities such as translocations to activate oncogenes, or deletions to inactivate suppressor genes.

Evidently, abnormal MEs and chromosomal abnormalities to cause activation of oncogenes or inactivation of suppressor genes are very critical issues of cancer, responsible for perpetual proliferation of CCs which is the most outstanding feature of cancer. Abnormal MEs and the collapse of chemo-surveillance are responsible for the blockade of differentiation, and chromosomal abnormalities are responsible for the promotion of cell replication. Chromosomal abnormalities received a lot of attention. Cancer establishments devoted exclusive attention to develop gene therapy during the 20 years period between 1976-1996 right after the unsuccessful attempt to win the war on cancer declared by President Nixon in 1971 [29]. Entire human genomes were sequenced in a preparation to develop gene therapy. They gave up, because it was simply too difficult and too expensive to develop gene therapy. Additionally, it was not feasible to develop gene therapy due to the difficulty to control chromosomal abnormality consecutively throughout. Abnormal MEs are the most critical issue of cancer [30], which show up in PSCs, the precursors of CSCs, and pass on to CSCs and CCs.

The abnormal MEs are commonly shared by all human cancers [31]. A stroke to eliminate abnormal MEs can also resolve problems attributable to chromosomal abnormalities. After all, oncogenes and suppressor genes are cell cycle regulatory genes. These genes have important roles to play when cells are in cell cycle replication, though if replicating cells exit the cell cycle to undergo terminal differentiation, these genes have no roles to play. It appears that the solution of abnormal MEs can also achieve the effects of gene therapy which is otherwise very difficult to accomplish. Killing of CCs can also resolve issues attributable to abnormal MEs and chromosomal abnormalities. It has been tested, but failed. Abnormal MEs are definitely the bullseye of cancer target [32]. Cancer

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establishments were very close to the establishment of cancer therapy to target abnormal MEs. Aberrant tRNA methylation was aggressively pursued during a few years span around 1966, and aberrant DNA methylation was aggressively pursued during a few years span around 1985.

They looked into the wrong directions to analyze methylated nucleic acids. Had they focused the attention on abnormal MEs, cancer would have possibly been solved in these two periods.

II.2 Cancer Evolves as a Consequence of Wound Failed to Heal

In the previous section, we have briefly described the evolution of cancer due to wound unhealing, resulting in the evolution of PSCs to CSCs, and then the progression to faster growing CCs. The concept of cancer evolving due to wound unhealing was first introduced by the great German scientist Virchow in the 19th century [33]. It was again brought up by Dvorak in 1986 [34]. The close relationship between cancer and wound healing was noticed by MacCarthy-Morrough and Martin [35]. We provided the most important details on this subject which included abnormal MEs to promote perpetual replication of CCs [8, 11-13, 31]; chemo-surveillance as the nature's creation of allosteric regulation to ensure perfection of wound healing [21-24]; DIs and DHIs as wound healing metabolites and as active players of chemo-surveillance [21-24]; hypomethylation of nucleic acids as a critical mechanism on the induction of terminal differentiation of cells with abnormal MEs [36]; mechanism of wound healing to involve the proliferation and the terminal differentiation of PSCs [16, 29, 37, 38]; and the evolution of CSCs from PSCs through a single hit to silence TET-1 enzyme [27,28,39]. These studies strongly support the concept that cancer evolves as a consequence of wound failed to heal. Our carcinogenesis studies confirmed the validity of this concept. During the challenges with hepatocarcinogens, we noticed numerous tiny hyperplastic nodules appeared before the appearance of large size carcinomas [40]. These preneoplastic hyperplastic nodules must represent proliferation of PSCs in the process of active wound healing, most of which disappeared shortly afterward, which was an indication of the completion of wound healing. Only the tiny hyperplastic nodules which was not healed later developed to become large size carcinomas. If Antineoplaston A10 was administered during the challenge with potent hepatocarcinogen aflatoxin B_1, the development of carcinomas could be effectively prevented. Antineoplaston A10 is phenylacetylglutamine, which is an effective anti-cachexia chemical to protect the integrity of chemo-surveillance [23]. So, wound healing and cancer are closely related.

Wound healing is a simple matter, which comes naturally without having to put up any effort. Take surgical wound for example, suture and application of antibiotics are subsidiary to speed up and to prevent infection. The nature creates chemo-surveillance and immuno-surveillance to ensure perfection of wound healing. Chemo-surveillance is to heal wounds caused by toxic chemicals including carcinogens or physical means and immuno-surveillance is to heal wounds caused by infectious agents. Chemo-surveillance and immuno-surveillance can be synergistic to heal wounds by eliminating different origins of wounds, but can also be antagonistic. Immunological response tends to trigger the production of cytokines to cause the collapse of chemo-surveillance. immuno-surveillance can hurt chemo-surveillance, but chemo-surveillance cannot hurt immuno-surveillance. White lung observed during COVID-19 infection is the buildup of PSCs in the process of wound healing unable to undergo terminal differentiation because of the collapse of chemo-surveillance following active immuno-logical response to COVID-19 infection.

Wound healing is a simple matter. Likewise, cancer therapy can also be a simple matter, if the therapy follows the process of wound healing. Obviously, the functionality of chemo-surveillance is very critical to dictate the success of wound healing [21-24]. Chemo-surveillance has to be

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damaged for cancer to set in. The progress of cancer further contributes to the damage of chemo-surveillance. The progress of cancer invites immunological response that yields TNF to cause cachexia symptoms leading to the damage of chemo-surveillance. Cytotoxic agents and immunologic agents cause the acceleration of the damage to chemo-surveillance. Ineffectiveness against CSCs and the contribution to the damage of chemo-surveillance are the reason cytotoxic chemotherapy failed to win the war on cancer.

Cancer therapy following the process of wound healing displays the feature as pro-wound healing, which is the right indication of cancer therapy because cancer evolves due to wound unhealing.

Cancer therapy mediated through cytotoxic agents and immunological agents display the feature as anti-wound healing, clearly the contra-indication of cancer therapy. A right approach is the magic code to the success of solving tough challenges [42], but a wrong approach cannot solve a simple matter as cancer and supported as a presidential project [43].

II.3 CDA Formulations as Persuasive Good Cancer Drugs

Cytotoxic chemotherapy of cancer was a tragic by product of World War II. During the war toxic sulfur mustard gas bombs were used. Victims of toxic gas all displayed depletion of leukocytes in their blood specimens, which inspired oncologists to employ toxic chemicals to treat leukemia patients. Toxic chemotherapy became the standard care of cancer, and the disappearance of cancer cells or tumor became the standard criteria for the evaluation of therapeutic efficacy. These were tragic mistakes made at a time when we did not have complete knowledge of cancer.

Chemotherapy and radiotherapy were the major therapeutic modalities employed to combat cancer when President Nixon declared war on cancer in 1971. But this presidential project was not successful [43]. If a treatment modality was drilled through as a presidential project and failed, it was fair to conclude that the treatment modality was not good. Apparently, cancer establishments agreed to such conclusion, and immediately shifted the development of cancer therapies from cytotoxic chemotherapy to gene and targeted therapies during 1976-1996, to anti-angiogenesis during 1996-2016, and then to immunotherapy from 2016 onward [29]. They did not develop acceptable therapy good enough to replace chemotherapy, as the commanding principle was still based on cell killing and the disappearance of tumor. Cytotoxic drugs and radiation remain the dominant cancer drugs to contribute to ever increasing cancer mortality to more than 10 million annual deaths worldwide [5]. Immunotherapy is definitely better than chemotherapy. It is selective against cancer cell surface antigens. Hopefully, it can replace DNA interacting drugs to reduce toxicity. But it still has the same problem of chemotherapy to create damage to chemo-surveillance and to show ineffectiveness against CSCs. The antigenicity of CSCs is exactly the same as that of PSCs, which is tolerable to human immune systems.

A perfect cancer drug must be able to take out both CCs and CSCs, and to restore the functionality of chemo-surveillance [44]. Although CSCs constitute only a small sub-population less than 2% of the mass of most primary cancers, CSCs actually contribute the major fatal effects of cancer. Fatal effects of cancer such as metastasis, recurrence, drug resistance, and angiogenesis are the making of CSCs. Thus, elimination of CSCs is essential to save cancer patients [45]. Cancer drugs put up by cancer establishments cannot access CSCs which are protected by drug resistance and anti-apoptosis mechanisms. These drugs can only benefit early stage cancer patients whose chemo-surveillance has not yet been fatally damaged, relying on the recovery of chemo-surveillance to subdue surviving CSCs. Chemo-surveillance of advanced patients is often badly damaged beyond recovery. CSCs population of advanced patients, particularly the patients undergoing long term chemotherapy, is much higher than early stage patients. Such patients cannot respond to cytotoxic drugs. If still responsive to reach complete remission, these patients are very likely

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to recur and become unresponsive to further treatment. CSCs are a dominant issue of metastatic, unresponsive and recurrent cancer patients. CSCs like PSCs are closely linked to wound healing which is a major biological mission of these cells. Induction of terminal differentiation is the only option to eliminate CSCs [45]. Killing cannot solve the problem related to CSCs. Therefore, CDA formulations made up by DIs and DHIs are the best drugs to handle CSCs [39, 45].

Myelodysplastic syndromes (MDS) are unique diseases caused by the propagation of CSCs [46]. These diseases are a show case to demonstrate the evolution of CSCs due to immunological disorder to trigger production of TNF resulting in the collapse of chemo-surveillance [25, 26]. Antibody to TNF can prevent the progression of the disease. Thus, TNF is responsible for the development of MDS. On one hand, it causes excessive apoptosis of bone marrow stem cells, thus severely affect the ability of the patient to produce hematopoietic cells such as erythrocytes, platelets or neutrophils.

On the other hand, it increases vascular permeability to result in excessive excretion of low molecular weight metabolites [47, 48]. DIs and DHIs of wound healing metabolites are among low molecular weight metabolites excreted to result in wound unhealing that forces evolution of CSCs from PSCs. The propagating pathological cells have been identified as human CSCs [46].

Therapy of MDS requires the induction of the terminal differentiation of CSCs to become functional erythrocytes, platelets or neutrophils. Killing of CSCs cannot heal MDS. So far, Vidaza, Decitabine and cell differentiation agent-2 (CDA-2) are the three drugs approved for MDS therapy by the Chinese FDA. CDA-2 is our creation, which was wound healing metabolites purified from freshly collected urine [49]. Vidaza and Decitabine are also approved for MDS therapy by the US FDA. Professor Jun Ma, Director of Harbin Institute of Hematology and Oncology, was instrumental to conduct clinical trials of all three MDS drugs in China. According to his assessments based on two cycles of treatment protocols, each cycle lasting 14 days, CDA-2 had a noticeably better therapeutic efficacy based on cytological evaluation, and a markedly better therapeutic efficacy based on hematological improvement evaluation, which was an evaluation based on the dependence of blood transfusion [50]. All three drugs achieve MDS therapy by inactivation of abnormal MEs, Vidaza and Decitabine by the covalent bond formation between DNA methyltransferase and 5-aza-cytosine base incorporated into DNA to eliminate MT [51], whereas CDA-2 destabilizes abnormal MEs by the elimination of telomerase [12]. The action of CDA-2 is selective on the cancer target of abnormal MEs, whereas the action of Vidaza and Decitabine is non-selective that can also eliminate MT of normal stem cells. CDA-2 is devoid of adverse effects, whereas Vidaza and Decitabine are proven carcinogens [52, 53] and very toxic to DNA [54-56]. CDA-2 is obviously a drug of choice for the therapy of MDS with better therapeutic efficacy and devoid of adverse effects. It appears that CDA-2 is the only drug that can be characterized as a perfect cancer drug. The development of perfect cancer drugs should follow the hints revealed by CDA-2. CDA-2 contains DIs and DHIs as major ingredients to fight cancer. DIs are most like the degradation products of erythrocytes in the forms of liposomal complexes, which we assigned the name as OA-0.79, containing active DIs as fatty acids such as AA, dicycloPGs in association with pregnenolone [57, 58], and membrane fragments, which we assigned the name as PP-0, containing OA-0.79 in association with membrane fragments [57, 58].

Since the profile of plasma peptides and the profile of peptides extracted from the spleen were similar, we believed that plasma peptides were the degradative products of erythrocytes since the spleen was the organ known to process dead erythrocytes [59]. Uroerythrin is an important active DHI component of CDA-2 [49], which is definitely a degradation product of heme from hemoglobins. So, we believe catabolism of erythrocytes is an important source of active components of chemo-surveillance. Steroid metabolites are other important DHIs of CDA-2,

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which must come from organs involved in steroid metabolism. Human body produces important metabolites to heal wound, which are also the best cancer drugs, showing effectiveness and without adverse effects as demonstrated by the therapy of MDS with CDA-2 above described.

II.4 Development of CDA Formulations to Save Cancer Patients

Cancer evolves due to wound unhealing. Accordingly, the wound healing process provides the most appropriate modality of cancer therapy [60]. Indeed, wound healing process is the best strategy to cure cancer patients [61]. Cancer establishments may not be concerned with how many cancer patients die [6]. They think cancer patients are bound to die if untreated, they are happy to extent cancer patients' life a few years if the tumor disappear. Cancer establishments are focused on how to eradicate tumor to extent patients' life. The drugs used in therapies to eradicate tumor are also the drugs to kill cancer patients. Therefore, cancer mortalities continue to increase. It takes authorities above cancer establishments to save cancer patients. We rely on the Royal Family's supreme authorities to rectify cancer therapies to save cancer patients. CDA formulations are the only drugs that can take care of CSCs because induction of terminal differentiation of CSCs is the only option to solve CSCs [39, 44, 58, 62]. Vidaza and Decitabine can also solve CSCs, but these two drugs have to be incorporated into DNA to be effective [51]. They also damage DNA of normal stem cells to create destruction. Cancer establishments choose to continue to use drugs that damage the DNA of cancer cells to kill cancer cells, but these drugs also kill normal stem cells resulting in the death of cancer patients. Cancer establishments are the bosses. It takes authorities higher than the bosses of health profession to rectify the mistakes of bosses of health profession. The mistakes of cancer establishments are very likely to create damages to royal family's cancer. They have the authority to rectify damaging therapies. The right therapy of cancer is to eliminate CSCs by CDA formulations, which is tightly linked to wound healing. The elimination of CCs can be done by CDA formulations or cell killings, which is not so closely linked to wound healing. CDA formulations have an issue of residual tumor to deal with, albeit a harmless issue. If it is a worry concern, surgical removal of the residual tumor mass can solve the concern without having to worry on cancer metastasis because patients have the chemo-surveillance restored to prevent that from happening. Cell killings have adverse effects to deal with, which are often fatal, such as unresponsiveness and recurrence. Obviously, CDA formulations have the advantage over cell killings to save cancer patients.

We have carried out extensive studies of natural and unnatural DIs and DHIs for the establishment of CDA formulations for cancer therapy [19, 49, 57, 58, 63-68]. Our findings of effective DIs and DHIs are summarized in Table 1 and 2. On effective DIs, ATRA is the standard therapeutic drug of acute promyelocytic leukemia [69]. It requires the expression of the receptor of ATRA, namely RAR, to activate oligoisoadenylate synthetase to produce oligoisoadenylate as DI to achieve the therapeutic effect [70]. Other DIs listed in Table 1 work directly on abnormal MEs.

AA and its metabolites PG derivatives are natural DIs involved in chemo-surveillance. PG derivatives are approved drugs for the delivery. BIBR-1532 and boldine are approved cancer drugs as telomerase inhibitors. Development of CDA formulations is an application of new drugs which may take more than 10 years of clinical trial to get approval to save cancer patients. Change of indication does not take as long as new drug to the rescue of cancer patients. There are many approved drugs as DIs and DHIs, which can be used to establish CDA formulations right away to save cancer patients.

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Table 1: Effective DIs

DIs	ED_{25} (μM)	ED_{50} (μM)	ED_{75} (μM)
ATRA	0.18	0.36	0.75
PGJ2	7.9	13.8	20.5
PGE2	20.6	32.0	46.5
AA	21.0	42.0	-
Dicyclo-PGE2	21.0	43.5	-
BIBR1532	32.3	43.7	55.1
Boldine	80.1	78.7	94.2

Table 2: Effective DHIs

SAHH Inhibitors	$RI_{0.5}$ (μM)
Pyrvinium Pamoate	0.012
Vitamin D_3	0.61
Dexamethasone	0.75
Beta-sitosterol	1.72
Dihydroepiandrosterone	1.79
Prenisolone	2.22
HYdrocortisone	4.59
Pregnenolone	7.16
MT Inhibitors	**$RI_{0.5}$ (μM)**
Uroerythrin	1.9
Hycanthone	2.1
Riboflavin	2.9
MAT Inhibitors	**$RI_{0.5}$ (μM)**
Indol Acetic Acid	220
Phenylacetylvaline	500
Phenylacetylleucine	780
Butyric Acid	850
Phenybutyric Acid	970

Signal Transduction Inhibitors	$RI_{0.5}$ (μM)
Sutent	0.28
Berberine	1.62
Votrient	10.1
Gleevec	11.9
Selenite	19.7
Polyphenols	**$RI_{0.5}$ (μM)**
Tannic Acid	0.37
EGCG	0.62
Resveratrol	1.16
Curcumin	1.24
Kuromanin	1.43
Coumestrol	1.95
Genisteine	2.16
Pterostilbene	2.19
Pyrogallol	3.18
Silibinin	3.80
Caffeic Acid	3.87
Ellagic Acid	4.45
Gallic Acid	5.35

As shown in Table 2, SAHH inhibitors and MT inhibitors are better DHIs than MAT inhibitors.

MAT happens to be the largest molecule of MEs and the most stable enzyme of the three MEs. The association with telomerase further increases its stability. Therefore, it is relatively difficult to shake loose of this enzyme to help terminal differentiation of cells with abnormal MEs to achieve wound healing or cancer therapy. Signal transduction inhibitors as good DHIs are expected, since signal transductions tend to produce products to stimulate growth.

Polyphenols as good DHIs are a surprise, but is a good surprise. Polyphenols are regarded as good chemicals to maintain health, and promoted as healthy food. The activity of polyphenols as effective DHIs endorses the claim of polyphenols as healthy food. The breakdown of chemo-surveillance is due to the loss of DIs and DHIs the body produced. Supplement of effective DIs and DHIs is a good measure to restore the functionality of chemo-surveillance.

Pregnenolone is a major DHI of CDA-2 [58]. Apparently, pregnenolone is a major player of chemo-surveillance. It is the master substrate of

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steroid metabolites to have a great influence on growth regulation. The production of pregnenolone is bell shape in relation to ages with a peak daily production of around 50 mg at 20-25 years old [71]. The younger and the older people produce relatively little amount of pregnenolone, and these are two age groups most vulnerable to develop cancer. Pregnenolone is a single metabolite to greatly influence the evolution of cancer. It is our top choice of DHI to make CDA formulations.

Effective CDA formulations are made up by DIs and DHIs [19, 49, 57, 58, 63-68]. Effective CDA formulations can be ED_{25} of a DI + 3x $RI_{0.5}$ of a DHI, or ED_{50} of a DI + 2x $RI_{0.5}$ of a DHI, or ED_{75} of a DI + $RI_{0.5}$ of a DHI [58]. In the design of CDA formulations, we must take into consideration of non-cancer issues such as blood brain barrier of brain cancer, collagen envelop of pancreatic cancer and hypoxia of melanoma to select DIs and DHIs to overcome non-cancer issues. A lot of work remains to be done.

III. CONCLUSION

Cancer evolves due to wound unhealing. Pro-wound healing is the right approach of cancer therapy. Cancer establishments prefer anti-wound healing approach of cancer therapy to result in horrendous cancer mortality. Cancer establishments are obviously wrong to handle cancer issue. It takes authority higher than cancer establishments to rectify the mistake of cancer establishments. Recent cancer diagnoses of English royal family members, while a misfortune no body wishes to happen, offer a supreme authority to rectify cancer therapies to save cancer patients. CDA formulations are the correct solution of cancer.

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Conflict of Interest

The authors declare no conflict of interest.

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Total Ischemic Time has Prognostic Implications on Short Term Outcome of Primary Percutaneous Coronary Intervention (pPCI)

Md. Golam Morshed, Muhammad Azmol Hossain, Housneara Begum, Md Shamsuzzaman, Kazi Mohammed Zafrul Haq, Md. Mozammel Haque, Md. Khurshid Alam & Poppy Bala

ABSTRACT

Objectives: Primary percutaneous coronary intervention (pPCI) is being increasingly done as the treatment of acute ST elevation myocardial infarction (STEMI). Time until treatment is paramount in the management of STEMI. But the total ischemic time before pPCI how much influencing the outcome is a matter of interest. So we evaluated the influence of total ischemic time on myocardial reperfusion and short term clinical outcome in patients with STEMI treated with primary PCI.

Methods: This prospective observational study was conducted from August 2017 to July 2018 in the Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka.

Forty eight (48) acute STEMI patients were selected by purposive sampling based on inclusion and exclusion criteria dividing into two groups as short total ischemic time in whom pain to pPCI time was <6 hours and long total ischemic time in whom pain to pPCI time was 6-12 hours. Angiographic (TIMI flow grade 3 & MBG 3) & short term clinical outcome (MACE, heart failure, major bleeding, minor bleeding, cardiogenic shock, significant arrhythmia, instent thrombosis) were observed and compared between these two groups.

Keywords: total ischemic time, primary PCI (pPCI), prognostic implications.

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Total Ischemic Time has Prognostic Implications on Short Term Outcome of Primary Percutaneous Coronary Intervention (pPCI)

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Objectives: Primary percutaneous coronary intervention (pPCI) is being increasingly done as the treatment of acute ST elevation myocardial infarction (STEMI). Time until treatment is paramount in the management of STEMI. But the total ischemic time before pPCI how much influencing the outcome is a matter of interest. So we evaluated the influence of total ischemic time on myocardial reperfusion and short term clinical outcome in patients with STEMI treated with primary PCI.

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Results: The 30-day mortality & morbidity were assessed and compared between short and long total ischemic time before pPCI. The overall 30-day mortality rate was 4.2%, heart failure was 6.2%, cardiogenic shock was 4.2%, major bleeding was 2.1% and minor bleeding was 14.6%. Mortality and morbidity were higher in longer ischemic time group than shorter ischemic time group. In multivariate regression analysis, the factors independently influencing the adverse short term outcome were advance age (OR 1.51, 95% CI 1.105 to 4.101, p=0.03), hypertension (OR 2.44, 95% CI 1.102 to 4.281, p=0.02), diabetes mellitus (OR 2.51, 95% CI 1.200 to 4.987, p=0.02), anterior MI (OR 1.38, 95% CI 1.001 to 2.872, p=0.03), multivessel disease (OR 2.35, 95% CI 1.010 to 5.371, p=0.02), pain to door time (OR 1.66, CI 1.099 to 2.2.722, p=0.04), and total ischemic time (OR 2.67, 95% CI 1.122 to 5.784, p=0.02). Even after correction for predictive baseline and procedural variables of the univariate analysis, longer total ischemic time was the most significant independent predictor (OR 2.67, p=0.02) of short term adverse outcome of primary PCI.

Conclusion: According to this study finding, there is prognostic implication of total ischemic time in patients with STEMI undergoing primary PCI. Therefore, all efforts should be made to shorten total ischemic time, including reduction in patient related delays, to improve clinical outcome of STEMI patients.

Keywords: total ischemic time, primary PCI (pPCI), prognostic implications.

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I. INTRODUCTION

Coronary artery disease (CAD) is the most common form of heart disease and single most important cause of premature death in most part of the world. By the year 2020 it will become the major cause of death in all the region of the world.[1] Acute myocardial infarction (AMI) is one of the leading causes of death and disability. It generally occurs due to sudden occlusion of a coronary artery by formation of thrombus at the site of fissured or ruptured atherosclerotic plaque.[2] The resultant thrombus that is formed interrupts blood flow and leads to an imbalance between oxygen supply and demand, if this imbalance is severe and persistent, it leads to myocardial necrosis.[3] The major aspect of treatment of STEMI is reperfusion of the infarct related artery. Reperfusion therapy aims at restoration of antegrade flow in the occluded infarct related artery, which reduce infarct size and improves clinical outcome[4].

II. MATERIALS AND METHODS

This was a prospective observational study and was done in the department of cardiology in National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh from August 2017 to July 2018. Patients presented with acute STEMI admitted in CCU in National Institute of Cardiovascular Diseases who full filled inclusion and exclusion criteria were my study population. Sampling was purposive.

Considering nonresponse, unavailability of some respondent, inflation in the desired sample size is planned. Targeted sample size for the study = 40 + 8= 48. Study subjects were divided into two groups on the basis of time delay to reperfusion: Group A (shorter ischemic time): Patients whose symptom onset to first balloon/ stent time was < 6 hours were included in this group and Group B (longer ischemic time): Patients whose symptom onset to first balloon/ stent time was 6-12 hours were included in this group.

Patients presented within 12 hours of onset of typical chest pain with ST segment elevation in ECG and diagnosed as a case of acute STEMI (ST segment elevation myocardial Infarction) were included in this study. Patients having LBBB (left bundle branch block). Patients with history of old myocardial infarction. Patients who received thrombolytic therapy. Patients with high bleeding risk. Patients with valvular heart disease. Patients with cardiomyopathies Patients with established renal failure (S. Creatinine > 2mg/dl.). Patients with stroke. Patients with malignancy were excluded in this study.

All variables were entered into the Statistical Package for Social Sciences, version 16 (SPSS Inc., Chicago, Illinois). Data was presented as frequency and percents for categorical variables and as mean with standard deviation for quantitative variables. Paired t-test was done for quantitative variables where applicable.

Univariate and multivariate regression analysis were done with variables may be related to adverse outcome with calculated risk ratios & odds ratios [OR] for independent variables with 95% confidence intervals [CI]. P value <0.05 were considered as significant.

III. RESULTS AND DISCUSSIONS

This prospective observational study was conducted in the National Institute of Cardiovascular Diseases (NICVD), Dhaka during the period of August 2017 to July 2018. The main objective of this study was to assess the prognostic implication of total ischemic time on short term outcome of primary Percutaneous Coronary Intervention (PCI) among a case series of population presented with acute ST elevation myocardial infarction (STEMI).

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A total of 48 patients with acute ST elevation myocardial infarction who were consented to PCI were included in this study. Patients were classified as shorter total ischemic time (group-A) in whom treatment delay was<6 hours and longer total ischemic time (group-B) in whom treatment delay was 6- 12 hours. Two patients died at the same day of the procedure and all other patients were followed up in hospital and for one month.

Table I: Comparison of risk factors between early treatment group and late treatment group (n=48)

Variables	(Group A) n=23	(Group B) n=25	Total (n=48)	p value
Age in years	51.5±11.1	59.8±14.7	55.9±13.6	0.03^{s}
Hypertension	6 (26.1%)	14 (56.0%)	20 (41.7%)	0.03^{s}
Diabetes mellitus	7 (30.4%)	15 (60.0%)	22 (45.8%)	0.04^{s}
Dyslipidemia	11 (47.8%)	17 (68.0%)	28 (58.3%)	0.17^{ns}
Smoker	15 (65.2%)	20 (80.0%)	35 (72.9%)	0.25^{ns}

Group A: Total ischemic time <6 hrs. Group B: Total ischemic time 6 – 12 hrs. Quantitative data expresses in mean ±SD and qualitative data expresses in no. &(%). s= Significant (p<0.05), ns = Not significant (p>0.05) p value reached from Chi Square test.

The above table depicts the comparison of risk factors between early treatment group and late treatment group among the study population. Age, hypertension and diabetes were higher in patients with longer symptom onset to balloon time than in those with shorter symptom onset to balloon time and there were statistical significant association(p=0.03,p=0.03, p=0.04) respectively. Among the study population overall 41.7% were hypertensive, 45.8% were diabetic, 58.3% were dyslipidaemic and 72.9% were smoker.

Table II: Comparison of LVEF (%) between two groups before pPCI *(n=48)*

Group A (n= 23) LVEF (%)	Group B (n=25)		Total		p value (n=48)		
	Number	%	Number	%	Number	%	
≤ 35 (Severe)	0	0.0	0	0.0	0	0.0	
36 – 44 (Moderate)	2	8.7	7	28.0	9	18.8	
45 -54 (Mild)	20	87.0	17	68.0	37	77.1	
≥ 55 (Normal)	1	4.3	1	4.0	2	4.2	
Mean ± SD (Range)	48.4±3.9 (40-60)		46.1±4.7 (38-55)		47.2±4.4 (38-60)		0.06^{ns}

Group A: Total ischemic time <6 hrs. Group B: Total ischemic time 6 – 12 hrs. s = Significant (p<0.05), p value reached from unpaired t-test.

The above table displays that among early presenters (group A) 8.7% had moderate LV dysfunction and 87% had mild LV dysfunction but among late presenters (group B) 28% had moderate LV dysfunction and 68% had mild LV dysfunction before pPCI.

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Table III: Comparison of LVEF (%) between two groups after PPCI (n=48) Group A (n= 23)

Group A (n= 23) Group B (n=25) **LVEF (%)**	Total				p value (n=48)	
	Number	%	Number	%	Number	%
≤ 35 (Severe)	0	0.0	0	0.0	0	0.0
36 – 44 (Moderate)	0	0.0	0	0.0	0	0.0
45 -54 (Mild)	2	8.7	3	12.0	5	10.4
≥ 55 (Normal)	21	91.3	22	88.0	43	89.6
Mean ± SD (Range)	63.5±5.5 (50-70)		61.6±6.7 (46-70)		62.5±6.2 (46-70)	0.28^{ns}

Group A: Total ischemic time <6 hrs. Group B: Total ischemic time 6 – 12 hrs. s = Significant (p<0.05), p value reached from unpaired t-test.

The above table displays that after pPCI 91.3% patients had good LV function among those who are early presenter having total ischemic time <6 hours and those who are late presenter having longer total ischemic time (6-12 hours) among them 88% had good LV function

Table IV: Adverse outcomes between group A (early treatment group) and group B (late treatment group) (n=48) at one month

Adverse outcome	Group (n=23)		A Group (n=25)		B Total (n=48)		p value
	No.	(%)	No.	%	No.	%	
Death	0	0.0	2	8.0	2	4.2	0.49^{ns}
Heart failure	0	0.0	3	12.0	3	6.2	0.24^{ns}
Cardiogenic shock	0	0.0	2	8.0	2	4.2	0.49^{ns}
Major bleeding	0	0.0	1	4.0	1	2.1	0.69^{ns}
Minor bleeding	1	4.3	6	24.0	7	14.6	0.04^{s}

Group A: Total ischemic time <6 hrs. Group B: Total ischemic time 6 – 12 hrs. S= Significant (p<0.05), ns = Not significant (p>0.05) p value reached from Fisher's Exact test

The above table depicts that mortality in 1 month was 4.2%, heart failure was 6.2%, cardiogenic shock was 4.2%, major bleeding was 2.1% and minor bleeding was 14.6%. Most of the adverse outcomes occurred in late treatment group (6-12 hours from symptom onset to primary PCI) within one month. So it can be concluded that delay in symptom onset to balloon time (6-12 hrs) adversely affects the prognosis in patients with STEMI.

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Table V: Univariate logistic regression of adverse short term outcome of pPCI

Variables of interest	B	S. E.	p value	OR	95% CI
Advance age (>60 years)	0.368	0.431	0.02[s]	1.82	1.143-4.219
Male gender	0.152	0.101	0.30[ns]	1.24	0.057-1.541
Hypertension	0.589	0.379	0.01[s]	2.66	1.110-5.581
Diabetes mellitus	0.470	0.465	0.01[s]	2.78	1.110-3.811
Smoker	0.678	0.473	0.33[ns]	0.78	0.120-2.111
Anterior MI	0.439	0.351	0.02[s]	1.54	1.110-3.245
Multi vessel disease	0.578	0.354	0.01[s]	2.55	1.220-6.37
Lower LVEF (<45 %)	0.248	0.176	0.12 ns	1.99	0.494-2.872
Pain to door time	0.420	0.378	0.03[s]	1.92	1.071-2.824
Door to balloon time	0.119	0.101	0.31[ns]	0.99	0.110-1.780
Longer total ischemic time (6-12 hrs)	0.591	0.312	0.01[s]	2.97	1.154 – 7.889

Dependent variable: Adverse in-hospital outcome; Independent variables: Advance age, male gender, hypertension, diabetes mellitus, smoking, anterior MI, multi vessel disease, lower LVEF (<45%), pain to door time, door to balloon time and longer total ischemic time (6-12 hrs). s= Significant (p<0.05), ns= Not significant (p>0.05)

Above table demonstrates the binary logistic regression analysis of odds ratio (OR) for characteristics of the subjects likely to develop adverse short time outcome of primary PCI. The variables revealed to be significantly associated with univariate analysis were entered into the model directly. In regression analysis advance age, hypertension, diabetes mellitus, anterior MI, multi vessel disease, pain to door time and longer total ischemic time (6-12hrs) were found to be the significant predictors for developing adverse short term outcome of primary PCI.

Table VI: Multivariate logistic regression of adverse short term outcome of pPCI

Variables of interest	B	S. E.	p value	OR	95% CI
Advance age (>60yrs)	0.302	0.290	0.03[s]	1.51	1.105-4.101
Male gender	0.141	0.101	0.45[ns]	1.11	0.017-1.541
Hypertension	0.479	0.361	0.02[s]	2.44	1.102-4.281
Diabetes mellitus	0.435	0.304	0.02[s]	2.51	1.200 – 4.987
Smoker	0.220	0.119	040[ns]	0.88	0.111-2.509
Anterior MI	0.339	0.279	0.03[s]	1.38	1.001-2.872
Multi vessel disease	0.478	0.342	0.02[s]	2.35	1.010-5.371
Lower LVEF(<45 %)	0.232	0.107	0.27 ns	1.44	0.549-1.770
Pain to door time	0.410	0.301	0.04[s]	1.66	1.099-2.722
Door to balloon time	0.110	0.101	0.4 ns	0.88	0.120-1.699
Longer total ischemic time (6-12 hrs)	0.569	0.300	0.02[s]	2.67	1.122 – 5.784

Dependent variable: Adverse in-hospital outcome; Independent variables: Advance age, male gender, hypertension, diabetes mellitus, smoking, anterior MI, multi vessel disease, lower LVEF (<45%), pain to door time, door to balloon time and longer total ischemic time (6-12 hrs). s= Significant (p<0.05), ns= Not significant (p>0.05)

Above table demonstrates the binary logistic regression analysis of odds ratio (OR) for characteristics of the subjects likely to develop adverse short time outcome of primary PCI. The variables revealed to be significantly associated with multivariate analysis were entered into the model directly. In regression analysis advance age, hypertension, diabetes mellitus, anterior MI, multi vessel disease, pain to door time and longer total ischemic time (6-12hrs) were found to be the independent predictors for developing adverse short term outcome of primary PCI with

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ORs being 1.51, 2.44, 2.51, 1.38, 2.35, 1.66 and 2.67 respectively.

In multivariate analysis, we adjusted for potential confounders associated with the endpoints in univariate analysis. After correction for predictive baseline and procedural variables of the univariate analysis, longer total ischemic time was found as the most significant independent predictor (OR 2.67, p=0.02) of short term adverse outcome of primary PCI.

Reperfusion therapy (either mechanical or pharmacologic) is indicated for patients with chest pain with a duration of 12 hours or less in association with ST-segment elevation greater than 0.1 mV in two or more contiguous electrocardiographic leads or a new (or presumed new) left bundle-branch block. Early, effective and sustained reperfusion of the culprit artery is needed to salvage myocardium, maintain left ventricular function, and reduce mortality[5]. Primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy for ST-segment elevated MI (STEMI) when it can be performed in a timely manner by experienced personnel[6]. PCI for the treatment of STEMI was first reported by Hartzler[7]. Primary PCI in the late eighties only comprised balloon angioplasty, resulted better survival of patients when compared with thrombolytic therapy; however the introduction of intracoronary stents showed much better clinical outcome as compared to balloon angioplasty only[8]. If high-quality PCI is available, multiple randomized trials have shown enhanced survival compared to fibrinolysis with a lower rate of intracranial haemorrhage and recurrent myocardial infarction (MI)[9].

According to ACC/AHA guidelines for the treatment of STEMI patients, the time from medical contact to PCI (door-to-balloon time) should be 90 minutes and recommends a total ischemic time within 120 minutes[10]. Compared to fibrinolysis, primary PCI restores more often angiographically normal flow, including optimal TIMI 3 flow and blush, and has additional importance in patients with a contraindication for fibrinolysis[11-15]. Moreover, about a quarter of patients receiving fibrinolytic therapy has reocclusion of the infarct-related artery within 3 months after the myocardial infarction, with a recurrent infarction, which is very rare after primary PCI[16]. Therefore, Primary percutaneous coronary intervention (PCI) is generally preferable to fibrinolytic therapy when time until treatment is short. Each 30-minute delay from symptom onset to Primary percutaneous coronary intervention (PCI) increases the relative risk for 1 year mortality by 8%[17].

However, effects of early reperfusion have been difficult to determine in STEMI patients undergoing primary PCI, with several published studies showing widely different treatment effects of early as compared to late reperfusion. While some studies have reported no effect on infarct size with shorter symptom-to-PCI timings[18,19]

In our study, after correction for predictive baseline and procedural variables of the univariate analysis, longer total ischemic time was found as the most significant independent predictor (OR 2.67, p=0.02) of short term adverse outcome of primary PCI.

IV. LIMITATION OF THE STUDY

Although the result of this study supports the research question, there were some limitations of this study. These are, as the, sample size was small, it was difficult to generalize the findings to the reference population. Non randomized sampling done. Single centered study which didn't represent the status of the whole population. Short term observation. Angiography was evaluated by visual estimation, so there was chance of inter observer and intra observer variation of interpretation of the TIMI flow and MBG.

V. CONCLUSION

The results of this study strongly support the prognostic implication of total ischemic time in patients with STEMI undergoing primary PCI. Therefore, all efforts should be made to shorten total ischemic time, including reduction in patient related delays, to improve clinical outcome of STEMI patients.

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Proximate and Distance Heterosexual Dating Relationships: Differences, Similarities, and Dynamic of Factors that Predict Relational Success

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ABSTRACT

A data set of 1286 heterosexual dating individuals, grouped into 643 couples (406 couples in a Proximate relationship; 237 couples in a Distance relationship), were employed to explore Proximate/Distance similarities and differences in the dynamic of factors that predict relational satisfaction between couples. The primary dependent variable, couple relational satisfaction, was measured with eight items from the GWS and three items from the KMS. Primary predictor variables included eight composite variables (relationship satisfaction, emotional engagement, emotional regulation, family & friend support, shared activities, accuracy of perception, positive illusions, identity, and compatibility). Several individual variables were also employed, including loneliness, separation, permanence, enjoyment of sex, nurturance, disclosure, emotional stability, co-dependence, and others.

Keywords: distance relationships, proximate relationships, couple relationship satisfaction, structural equation modelling, accuracy of perception, emotional engagement, emotional regulation.

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Proximate and Distance Heterosexual Dating Relationships: Differences, Similarities, and Dynamic of Factors that Predict Relational Success

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Abstract

A data set of 1286 heterosexual dating individuals, grouped into 643 couples (406 couples in a Proximate relationship; 237 couples in a Distance relationship), were employed to explore Proximate/Distance similarities and differences in the dynamic of factors that predict relational satisfaction between couples. The primary dependent variable, couple relational satisfaction, was measured with eight items from the GWS and three items from the KMS. Primary predictor variables included eight composite variables (relationship satisfaction, emotional engagement, emotional regulation, family & friend support, shared activities, accuracy of perception, positive illusions, identity, and compatibility). Several individual variables were also employed, including loneliness, separation, permanence, enjoyment of sex, nurturance, disclosure, emotional stability, co-dependence, and others. A crisscross technique (rate self and partner across all variables) facilitated many comparative procedures. Correlations, t-tests, regressions, and structural equation modeling contributed toward the final picture. Results indicate that (a) Distance couples boast a healthier overall personal and couple profile; (b) accuracy of perception plays a larger role for Distance couples than for Proximate; (c) nurturance follows a similar pattern with a greater impact for Distance couples; (d) family & friend support plays a larger role in Proximate relationships; (e) emotional regulation plays a larger role for Proximate couples; (f) enjoyment of sex is a significant predictor for Proximate couples but not for Distance; and (g) loneliness, highly characteristic of Distance relationships, does not have a negative impact on relational success for Distance couples but significantly diminishes relational satisfaction for Proximate couples. Findings are discussed and avenues for future research explored.

Keywords: distance relationships, proximate relationships, couple relationship satisfaction, structural equation modeling, accuracy of perception, emotional engagement, emotional regulation.

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Introduction

In every era, circumstances have often forced romantic relationships to be maintained at distance, and the liabilities of such relationships have been endlessly discussed and agonized over. Over time, two foundational contrasting theories have emerged about the potential benefits or liabilities of distance relationships. Theory #1 states that distance relationships are at greater risk (than their proximate counterparts) because, due to lack of much contact, partners develop positive illusions about each other that contrast sharply with reality. Theory #2 states that Distance relationships are healthier because partners must work much harder to ensure Relational Success. Psychological research has explored both theories to understand the merits of each (e.g., Mietzner, 2005; Sahlstein, 2004; Waterman, 2017; Acost-Rodas et al., 2020; Stafford, 2010; Suwinyattichaiporn et al., 2017).

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The results have been mixed, leading to the primary purpose of the present study.

We pause a moment to operationalize our terms. A "Proximate" relationship is one in which the partners are in the same geographic location, close enough that daily in-person contact is possible. A "Distance" relationship is one in which the partners are geographically at a distance in which daily in-person contact is not possible. For clarity, the terms Proximate and Distance are capitalized throughout the paper.

The topic of Distance relationships has occupied a good deal of academic attention. However, differences *between* Proximate and Distance relationships have not been so heavily explored. Past studies frequently select a sample of individuals (or couples) in a long-distance romantic relationship and then explore topics such as (a) the impact of technology on communication patterns (Acost-Rodas et al., 2020; Wang et al., 2019), (b) the use of social media in supporting relationships (Billedo et al., 2015; Gutzmann, 2018; Zamanifard & Freeman, 2019), (c) the impact of social media on the increase of distance relationships (Acosta-Rodas et al., 2020), (d) the facilitation of personal growth when partners are at distance (Mietzner, 2005; Sahlstein, 2004; Waterman et al., 2017), (e) the importance of peer support (Roberts, 2003; Westefeld & Liddell, 1982), (f) the impact of attachment styles (secure, insecure, avoidant) on Relational Success (Pistole et al., 2010; Roberts & Pistole, 2009; Williams, 2021), (g) the problem of idealization and positive illusions in distance relationships (Stafford & Merolla, 2007; Suwinyattichaiporn et al., 2017), (h) the impact of future planning on Relational Success (Sahlstein, 2006), (i) gender differences in adjusting to physical separation (Cameron & Ross, 2007; Helgeson, 1994; Henderson et al., 2023), (j) the quality and frequency of communication (Holt & Stone, 1988; Holtzman et al., 2021), (k) the impact of commitment in distance relationships (Gonzalez, 2011), (l) the impact of technology on sexual expression when at distance (Goldsmith & Byers, 2018; Kidwell, 2021), (m) the impact of relationships that were previously long distance on future marriage (Du Bois et al., 2015), (n) the fact that college students have a greater incidence of distance relationships than any other demographic group (Beckmeyer et al., 2021; Waterman et al., 2017), and (o) the importance of savoring past experiences for those at distance (Borelli et al, 2014).

Each topic was considered as authors crafted the present research. Whereas the previous paragraph identifies broad themes of general research in the domain of Distance relationships, only a limited number of studies attempted to identify differences between couples in Proximate and Distance relationships. A summary of such research follows.

Previous studies have found it difficult to identify differences between those involved in Proximate and Distance relationships. Often, differences found are either tautological (couples at Distance have less face-to-face communication), differences are not robust, or different studies end up with contradictory results. For instance, for the variable Relationship Satisfaction, results from literature are mixed. Some find that Distance couples are less satisfied (Horn et al., 1997), some indicate that there is no difference between Proximate and Distance in satisfaction (e.g., Peterson, 2014; Roberts, 2003; Guldner and Swensen, 1995; Goldsmith & Byers, 2018), and some find that Distance relationships are more satisfied (e.g., Stafford & Merolla, 2007; Borelli et al., 2014; Kelmer et al., 2013). Other findings support that Distance relationships (a) have less self-Disclosure (Van Horn et al., 1997); (b) have less companionship (Van Horn et al., 1997); (c) are more Lonely (Waterman et al., 2017; Firmin, Firmin & Lorenzen, 2000); (d) have higher dedication and commitment to the relationship (Beckmeyer et al., 2021; Kelmer et al., 2012); (e) have less intimacy (Greenberg & Neustaedter, 2012); (f) have more intimacy (Guldner & Swensen, 1995); (g) are more likely to use social media to communicate (e.g., Greenberg & Neustaedter, 2013; Holtzman et al., 2021; Zamanifard & Freeman, 2019); (h) do not differ from their Proximate counterparts on Sexual satisfaction (Goldsmith & Byers, 2018; Goldsmith and Byers, 2020); (i) experience a lower network

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of peer support (Parke et al., 2013); (j) have less mutual trust (Dainton & Aylor, 2002); (k) participate in more activities together (Greenberg & Neustaedter, 2013); (j) do not differ from Proximate relationships in frequency of conflicts and resolution of those conflicts (Beckmeyer et al., 2021; Cionea et al., 2018); and a few other individual findings.

The present research has two primary objectives. First is to explore differences in the dynamic of factors that predict Relational Success in Proximate and Distance relationships. The second is to gain a more holistic view of the interplay of such factors on Relational Success. As noted in research cited earlier, most studies address only a small segment of personal and interactive qualities that might contribute to (a) differences between Proximate and Distance couples or (b) factors associated with the success of those relationships. Gestalt psychologists argue that it is critical, from time to time, to step back and look at the complete picture. With the wide array of predictor variables employed in the present study, structural equation modeling assists in creating this "complete picture".

Challenges of Research in this Area

One challenge of finding Proximate-Distance differences is the arbitrary nature of the terms. The words "Proximate" and "Distance" only identify a physical reality. A couple who has dated for three years and been separated for two months find themselves in the same category as a couple who met online, are dating, and have never even met each other. The difference of acquaintanceship potential is substantial. In the present study, in addition to the categorical Proximate-Distance variable, we created a quantitative Acquaintance-Potential variable out of descriptive information from each participant.

A second challenge of working with dating couples is difficulties with the primary dependent variable, Relationship Satisfaction (abbreviated "RS" throughout the paper). Taylor and Brown (1988), in their much-publicized research, noted that positive illusions are alive and well in relationships. They documented that about 80% of people in almost any accomplishment or personal domain think they are above average. One author has measured marital satisfaction several times in studies with married couples, and Taylor and Brown are verified, in fact, exceeded. On a 7-point, multiple-item scale, 91.5% of married couples in these studies rate their relationships above "mid" (about as happy as other married couples) [George, Luo et al., 2015; George, Anderson et al., 2023; George, Lewis et al., 2023; George, Saugh et al. 2023]. The problem is compounded when dating couples rate their own relationship satisfaction. While the mean RS for married couples is 5.82 on a 7-point scale (from the same studies cited above), dating couples often average 6.5 on the same scale. In the present study, more than 99% of participants rated their Relationship Satisfaction greater than 4 (about as happy as other dating couples). This results in limited variability and psychometric distortion. In the Results section we discuss methods to resolve the problem.

The final issue is expected in any correlational study that attempts a comprehensive look with many variables; that is, the issue of multicollinearity or linear dependency. As the number of variables increases, the issue of multicollinearity becomes increasingly challenging (see George & Mallory, 2024 for a review). The first line of defense addressed our primary dependent variable, Relationship Satisfaction. Not only was our measure of Relationship Satisfaction highly internally consistent (α = .93), but also no questions that measure this construct are included as either predictor variables or as indicators of composite predictors. Then, there is the problem of intercorrelations between the many predictor variables. Regressions, partial correlations, factor analysis (both confirmatory and exploratory), and internal consistency measures (Coefficient alpha) are used to minimize intercorrelation between composite predictors. While it is impossible to eliminate multicollinearity, all statistical resources have been employed to minimize these challenges.

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Hypotheses

The authors felt that to document 20 or 25 different hypotheses would be distractive. In literature just cited, we anticipate (hypothesize) similar results where researchers agree. But the task of the study extends well beyond confirmation of hypotheses or replication of prior studies. We seek to move toward a more complete understanding of how the dynamic of factors that contribute to Relational Success operate differently in Proximate relationships and Distance relationships.

Method

Initially, 2,030 individuals opened the link that accessed the questionnaire; 316 forms were deleted due to no data entered, incomplete data, or other irregularities. Of the remaining 1,714 participants, 1,286 (643 couples) fit the required criteria of "dating, heterosexual couples". Those who did not fit this criterion were not included in analyses. Participants originated from 44 U.S. states and 13 foreign countries. The ethnic breakdown of the sample was 84% White, 7% Black, 6% Hispanic, 2% Asian, and 1% Other. The mean age of the sample was 21.1 years with a range of 18 to >44 years. The mean length of the relationship was 1.8 years with a range of 1 month to >3 years. Education levels averaged about 2.3 years of university (range: <*HS* - *doctorate*).

This study was approved by the university Institutional Review Board prior to data collection.

Materials

Materials included separate but identical questionnaires for the subjects and partners. The survey was crafted with gender-neutral wording allowing men and women to complete the same form. Questionnaires were administered to all participants through an internet link to a Qualtrics survey.

The questionnaires were structured in the following way: The initial screen identified the sponsoring organization, provided a brief description of the study, assurance of anonymity, informed consent, debriefing, and further instructions about how to complete the questionnaire. Instructions were followed by 11 demographic items. After this, 39 randomly distributed questions assessed issues of emotional engagement, emotional regulation, destructive interactions, shared activities, and the support of family and friends. The next set of questions assessed strength of essence qualities in 13 different areas, 4 questions dealt with modes of communication, 4 questions measured temperament, 12 items measured personality traits, and 17 questions assessed Relationship Satisfaction.

Of the 88 questions (following the demographic items), 10 of the questions were individual (asking the participant only their own perspective), and 78 (or 39 pairs) were paired so that participants answered the question about themselves and a parallel question assessing their partner on the same quality. This procedure employs crisscross methodology widely used in couples research (see Szinovacz & Egley, 1995 for a review). To illustrate, one question used in the study was "How good a listener are you when your partner speaks?" The man rated how good a listener he thinks he is and how good a listener he feels his partner is. The woman also answered the same question about herself and her partner. Crisscross techniques allow greater objectivity by averaging each subject's self-rating with the partner's rating of the subject. It also enables creation of variables that contrast the perspectives of the partners such as Accuracy of perception, Positive Illusions, and Compatibility.

Procedure

Participants were acquired by students enrolled in a research methods class at a large public university in Alabama for partial class credit. All students completed CITI certification successfully, thus qualifying them to collect data for projects designed for publication. Students contacted individuals they knew to ask their willingness to participate in the study. Contacts were made in person, by telephone, e-mail, or social media. Links were sent out to all who agreed to participate. Couples were instructed to complete

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the questionnaires separately. Clicking the link opened the questionnaire. When participants were finished, data was automatically forwarded to the Qualtrics database.

The final data set provided anonymity for all participants. There was no identifying information in any of the questions posed, and the data file was password protected so that only the researchers had access to it. Acquisition of participants by students provided unique potential for biases or invalid forms. The authors used many resources (time to complete the form, missing data, irregular responses, identical forms, and others) to ensure all data analyzed came from valid participants.

Variables

There are many individual and composite variables involved in this study. To streamline the paper, we provide a "Variables" section that includes some components of both the Method and Results. Common to any Method section, we identify how variables are crafted and measured. In addition, several of the composites are mathematically complex and often involve factor analysis to support their creation. By incorporating mathematical underpinnings into this section, all composite variables are reported in one location and in order. Table 1 summarizes the variables created, indicators involved, measures of internal consistency (when applicable), and lists of standard psychometrics.

Defined terms: A "*criss-crossed"* variable refers to the mean of the self-rating of the subject and the partner-rating of the subject. A *"couple-specific"* variable (or composite) identifies questions that refer to the couple as a unit, such as "how often do the two of you have a stimulating exchange of ideas?" A *"gender-neutral"* variable refers to composite variables that includes both the male and the female perspectives. Factor analysis suggested that Emotional Engagement and Emotional Regulation are qualities that don't exist in isolation but require a dynamic between both partners. Hence, both these variables are designated as gender-neutral. For clarity, all variable names are capitalized. Example: emotional engagement is measured by the variable "Emotional Engagement".

Relationship Satisfaction (men and women): The primary dependent variable was a composite of two different relationship-satisfaction questionn-aires: The 8-item George-Wisdom Relationship Satisfaction Scale (GWS) (George & Wisdom, 2016) and the 3-item Kansas Marital Satisfaction Scale (KMS) (Schumm et al., 1983). The George-Wisdom scale asks questions about eight specific areas that measured Relationship Satisfaction, including: security, feeling loved, experience of joy, appreciation, trust, respect, enjoyment of activities, and fun & laughter. The KMS asks three global questions about satisfaction with the relationship, satisfaction with their partner, and how well the partner fulfills their needs. All 11 items were assessed on 7-point scales; anchors varied based on the nature of the questions. The final measure of RS was the mean of the 11 items. These 11 questions, with a mix of specific and global, yielded excellent internal consistency (alphas of .93 for both men and women).

Variables Created From Qualitative Material: Three *quantitative* variables were created from *qualitative* questions. Participants were asked to identify how they met, when the relationship began, and the pattern of separate or together time during their relationship. These new quantitative variables were created and measured based on the assessment and consensus of three of the authors.

***How they met*:** This identified and assigned the way the couple met to 11 different categories (e.g., online, at a party, known each other since childhood, in high school, etc.).

***Length of proximate time together*:** The when-they-began-dating information along with their pattern-of-separate-and-together-time identified how long they were actually in the same geographic location; deleting times when they were physically separated or not romantically involved. The final measure was simply the number of months in which their relationship was proximate.

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Acquaintance Potential (AQP): AQP was crafted from the how-they-met variable (e.g., "met online" would receive fewer points than "grew up together"), and the pattern-of-separate-and-together-time variable (greater amount of proximate time received higher credit). This variable was coded on a 7-point Likert scale with "1" indicating low AQP and "7" designating high AQP.

Other Predictor Variables: *Emotional Engagement (gender neutral).* (Note: "m/w" indicates the perspective of both men and women). The first composite was the mean of 12 crisscrossed variables: expressing Affection (m/w), expressing Verbal Love (m/w), expressing Feelings (m/w), using Love Languages effectively (m/w), understanding Emotional Needs (m/w), and supporting the Growth of their partner (m/w). Internal consistency: α = .90.

Emotional Regulation (gender neutral): The second composite was the mean of 12 crisscrossed variables and included: Patience (m/w), Criticism —reverse coded (m/w), Problem Resolution orientation (m/w), Looking for the Good in their partner (m/w), Listening skills (m/w), and the couple-specific variables: Frequency of Conflicts and skill at Resolving Conflicts. Internal consistency: α = .87.

Support: The men's and women's rating for Support of Friends and Support of Family. Internal consistency: α = .74.

Shared Activities: The mean of the five variables measured shared Activities; all activities were couple specific and involved (a) shared Projects, (b) Stimulating Exchange of Ideas, (e) shared Traditions, (d) Planning for the Future, and (e) number of Dates. Internal consistency: α = .66.

***Individual variables*:** A number of variables did not group well with other factors in the Factor Analysis structure. There were some surprises; for instance, enjoyment of the Sexual relationship did not factor in with Emotional Engagement. The following variables are included in analyses-all are crisscrossed, all are rated on 7-point scales with "1" representing less of the quality and "7" indicating more of the quality.

- Loneliness (men & women)
- Need for Space (men & women)
- Likelihood of Permanence of the relationship (men & women)
- Sexual enjoyment (men & women)
- High "I" temperament—Spontaneous, extroverted (men & women)
- High "S" temperament—supportive, Nurturing (men & women)
- Amount of self-Disclosure (men & women)
- Emotional Stability (men & women)
- Codependence (men & women)
- Face-to-Face communication (couple specific)
- Written communication (couple specific)
- Phone (audio) communication (couple specific)
- Zoom (audio and visual) communication (couple specific)

***The computed variables overview*:** The computed variables include Accuracy of perception for men and for women, Compatibility as measured by congruence of essence qualities (couple specific), Strength of Identity for men and for women, and Positive Illusions for men (viewing his girlfriend more positively than the girlfriend views herself), and women (viewing her boyfriend more positively than the boyfriend views himself).

Essence qualities are central to the computation of two variables; hence some explanation is required. The concept of essence qualities was first introduced to academic literature in 2020 (George, Wisdom et al.). These are qualities that identify the *contents* of the Identity of an individual. In the present study, 13 essence qualities are listed, and participants rated (on a 7-point scale) to what extent each quality defines them. For example, one of the 13 is "enthusiastic pursuit of fitness" with anchors of *Avoid activity at all cost* (1), to *moderately* (4), to *fitness enthusiast* (7). These ratings can be used to calculate the strength of Identity (the mean of the 13) or to construct a Personal Similarity Correlation (PSC) to identify how congruent the couple is on these essences. Essence qualities in this study include social, patient, cherish family

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and family events, growth orientation, spiritual, musical or artistic, neat, planful, fitness enthusiast, perceptive, risk-taker, humorous, and adventurous.

Compatibility: *PSC of the essence qualities (couple specific).* Personal Similarity Correlation (PSC) has gained visibility in the relationship -satisfaction literature in recent years (George, Luo et al., 2015; George, Wisdom et al, 2020; George, Anderson et al., 2023; Luo & Klohnen, 2005; Luo, Chen et al., 2008). A PSC involves the calculation of the correlation between constructs shared by both couples. In this study, it is the correlation between the 13 essence qualities that couples share. A negative correlation suggests that their essences contrast with each other—such as a professional musician married to someone who hates music. A zero correlation suggests that their essences are unrelated to each other. A positive correlation suggests that their essence qualities are shared—one measure of Compatibility. This variable ranges theoretically from -1 (*polar-opposites on all 13 qualities*) to +1 (*identical on all 13*). Actual PSC scores ranged from -.80 to .99.

Strength of Identity (men and women): For men and women respectively, this is the mean of the crisscrossed ratings of the 13 Essence Qualities. The rationale is that the higher the rating across these 13 contrasting qualities, the stronger their self Identity. This variable ranges theoretically from 1 (*lowest score on all 13*) to 7 (*highest score on all 13*). Actual strength-of-Identity scores ranged from 2.96 to 6.88 (men) and 3.04 to 6.71 (women). Internal consistency is irrelevant as the 13 variables are crafted as contrasting qualities.

Accuracy of perception (men and women): Accuracy measures were calculated for men and women. For all variables employed, Accuracy is the mean of the *absolute values* for (a) 38 variables that measure the man's rating of his girlfriend minus the girlfriend's self-rating; and (b) 38 variables that measure the woman's rating of her boyfriend minus the boyfriend's self-rating. See Table 1 for the formula. The objective is to measure how accurate the couples are at perceiving each other. All scores are positive and range from 0 (*identical perspectives*) to 6 (*polar-opposite perspectives*). Actual Accuracy of perception scores ranged from .11 to 2.49 (men) and .08 to 2.82 (women).

Enhancement (men and women): The impact of Enhancement (often referred to as "positive illusions") on Relationship Satisfaction has been heavily researched in the last few decades—with mixed results (e.g., Taylor & Brown, 1988; Neff & Karney, 2002; George, Wisdom et al., 2020). In this study, Enhancement was the mean of the sum of discrepancies (across all valanced variables) between the subject's self rating and the partner's rating of the subject. See Table 1 for the formula. A positive value indicated partner enhancement (rating the partner higher than the partner rated him or herself). A negative score referred to partner diminishment (rating the subject lower than the subject rates him or herself). A zero-value suggests neither enhancement nor diminishment. This variable theoretically ranges from -6 (*opposite negative ratings*) to +6 (*opposite positive ratings*). Actual Enhancement scores range from -2.21 to 1.58 (men) and -1.94 to 2.09 (women).

Results

Psychometrics of key predictor and criterion variables: There were 37 predictor variables. Psychometrics were excellent for 21 of those variables (skewness and kurtosis between ± 1), were acceptable for 13 of the variables (skewness and kurtosis between ± 2), and were problematic for two variables: Family & Friend Support (-1.68/2.16) and Written Communication (-2.22/3.64). See George and Mallory (2024) for a discussion of psychometric validity. No linear manipulations improved psychometrics of these two variables and the authors chose to include them in analyses with awareness of their limitations.

As noted in the introduction, the primary criterion variable, Relationship Satisfaction (RS), evidenced both severe skewness and kurtosis due to the large number of high ratings. The values with the initial data set resulted in a skewness of -2.39 and a kurtosis of 6.97. A first step was to

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replace missing values (fewer than 2%) with predicted values from regression equations. Next, frequency data indicated that there were 17 (out of 1286) that scored lower than 4.0. With a standard deviation of .8, a score of "1" would be *seven* standard deviations below the mean. A score of "4" is more than *four* standard deviations below the mean. As such, these low values are extreme outliers. To resolve this issue, the authors capped low scores at ≤ 4, that is, all values less than 4 were recoded to a single value of "≤ 4". No log manipulations improved the psychometrics. This process improved psychometrics to a skewness of -1.78 and a kurtosis of 2.66. Although not ideal, this was the dependent variable employed for men, women, and couple-satisfaction (the mean of the men's and the women's scores). See Table 1 for the psychometrics and method of construction of all primary variables.

The Influence of Demographics

For this section the entire data set is employed without making distinction between Proximate and Distance.

Gender differences: For gender differences that follow, all significance values are less than .001, $N = 643$. In this data set, women had greater Accuracy of perception [*M*s = 1.00 vs. 1.06, $t(642) = 6.89$], were more Lonely [*M*s = 3.15 vs. 2.80, $t(642) = -7.19$], wanted more Time Together [*M*s = 4.59 vs. 4.44, $t(642) = -4.15$], were more Nurturing [*M*s = 6.08 vs. 5.86, $t(642) = -5.92$], provided more self-Disclosure [*M*s = 5.81 vs. 5.44, $t(642) = -8.77$), and tended to be more Codependent [*M*s = 3.11 vs. 2.83, $t(642) = -8.24$]. Men enjoyed Sex more [*M*s = 6.52 vs. 6.32, $t(642) = 6.95$], and were much more Emotionally Stable [*M*s = 5.53 vs. 4.10, $t(642) = 20.99$].

Education: Level of education had a significant impact on a number of the predictors, all in the positive direction. The order of r- and p-values is men, then women. Results found that those with more education had greater Accuracy of perception [*r*s = -.08, -.12 *p*s = .02, .001], indicated greater likelihood of Permanence in the relationship [*r*s = .08, .09 *p*s = .02, .02], provided more self-Disclosure [*r*s = .14, .11 *p*s < .001, = .002], and were less Codependent [*r*s = -.09, -.09 *p*s = .01, .02]. Women had higher Emotional Stability [$r = .11$, $p = .002$]. There were no ethnic differences of interest.

Proximate-Distance Differences

The following are one-tail significant differences between Proximate and Distance couples based on Independent-samples t-tests. The "*d*" refers to Cohen's *d* and indicates how different (in standard deviations) mean values are for the two groups. To simplify statistical output, the degrees of freedom for all t-tests is 641. The first set of differences are so expected that they are essentially tautological: Note: M = men, W = women, C = couple. The *direction* of influence is noted in parentheses following each construct.

- C Dates: $t = 5.650$, $p < .001$, $d = .46$ (Proximate more dates)
- M Lonely: $t = -10.993$, $p < .001$, $d = -.90$ (Distance lonelier)
- W Lonely: $t = -11.916$, $p < .001$, $d = -.97$ (Distance lonelier)
- M Space from each other: $t = -17.447$, $p < .001$, $d = -1.53$ (Distance too much space)
- W Space from each other: $t = -17.592$, $p < .001$, $d = -1.50$ (Distance too much space)
- C Face-to-face communication: $t = 26.678$, $p < .001$, $d = 2.18$ (Proximate more f-t-f)
- C Writing: $t = -4.862$, $p < .001$, $d = -.36$ (Distance more writing)
- C Phone: $t = -3.126$, $p < .001$, $d = -.36$ (Distance more telephone)
- C Zoom: $t = -7.714$, $p < .001$, $d = -.63$ (Distance more zoom)

Otherwise, where there were differences, Distance relationships revealed a more positive profile than Proximate relationships across all significant comparisons. Although some of the differences are not strong (always $p < .05$) the superior profile of Distance relationships is 100%. Once again, degrees of freedom for all t tests is 641.

- RS men: $t = -1.91$, $p = .02$, $d = -.16$ (Distance more satisfied)
- RS women: $t = -2.04$, $p = .02$, $d = -.16$ (Distance more satisfied)

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- RS couple: t = -2.31, p = .01, d = -.18 (Distance more satisfied)
- C Length of relationship: t = -2.80, p = .003, d = -.23 (Distance longer)
- C Emotional Engagement: t = -2.24, p = .01, d = -.18 (Distance greater engagement)
- C Emotional Regulation: t = -1.86, p = .03, d = -.15 (Distance better regulation)
- M/W Strength of Identity: ts = -2.38/-3.18, ps = .009/<.001, ds = -.20/-.26 (Distance stronger identity)
- C PSC Compatibility: t = -2.06, p = .02, d = -.17 (Distance more compatible)
- M/W Permanence: ts = -3.30/-3.14, ps < .001, ds = -.26/-.25 (Distance permanence more likely)
- M/W Nurturing: ts = -2.05/-3.37, ps = .021/<.001, ds = -.16/-.26 (Distance more nurturing)
- M/W Disclosure: ts = -1.65/-2.22, ps = .05/.01, ds = -.14/-.18 (Distance more disclosure)
- M/W Codependent: ts = 1.76/2.01, ps = .04/.02, ds = .14/.16 (Proximate more codependent)

The Influence of the Acquaintance Potential Variable (AQP)

The Acquaintance Potential Variable was created from two qualitative variables: how the relationship began and the amount of time the relationship was proximate. The authors were hopeful that a continuous AQP would be more discerning in uncovering differences between couples than the categorical Proximate and Distance variable. The impact of AQP was not as strong as anticipated.

There were interesting correlations (when two values are reported, the men's value is first followed by the woman's). Combining both Proximate and Distance relationships, higher AQP was associated with greater likelihood of Permanence (rs = .278/.260, ps < .001), lower levels of Co-dependence (rs = -.153/-.177, ps < .001), more Activities (r = .239, p < .001), greater Family & Friend Support (r = .146, p < .001), greater Accuracy of perception (rs = -.08/-.07, ps = .025/.049), greater self-Disclosure for women (r = .070, p = .038), and greater Emotional Stability for men (r = .077, p = .026).

Predictors of Relationship Satisfaction, Bi- Variate Correlations

Since Relationship Satisfaction is the primary dependent variable, we report significant correlations between RS for men, RS for women, and RS for couples. Only correlations higher than .30 for all three RS measures (order: men, women, couple) are reported here. All significance values are p < .001, N = 643. Correlations are listed from high to low. Variables that rated high in bivariate correlations turned out to be major players in the final structural model.

The greatest predictor of RS is Emotional Engagement (rs = .61, .62, .70); this was followed by Emotional Regulation skills (rs = .55, .59, .65); then, Family & Friend support (rs = .50, .56, .61); shared Activities (rs = .43, .41, .48); women Accuracy of perception (rs = -.43, -.43, -.49); men Accuracy of perception (rs = -.42, -.34, -.43). A quick note: the negative values indicates that *deviation* from Accuracy hurts the RS. The woman's rating of the Permanence of the relationship (rs = .42, .42, .48); the woman having high Nurturance (rs = .40, .32, .41); the man's rating of the Permanence of the relationship (rs = .38, .34, .42); the woman's self-Disclosure (rs = .36, .33, .39); the man's enjoyment of the Sexual relationship (rs = .35, .32, .38); the woman's enjoyment of the Sexual relationship (rs = .32, .30, .35); and the man having high Nurturance (rs = .31, .33, .37).

An interesting contrast for a variable that did not achieve greater than .3 in all categories is Positive Illusions: For men with Positive Illusions (rating his girlfriend higher than the girlfriend rated herself) the correlation with his RS was strong and positive (r = .39, p < .001), but his girlfriend had a significant negative response (r = -.07, p = .045). For women with positive illusions (rating her boyfriend higher than the boyfriend rated himself) the correlation with her own RS was also strong and positive (r = .32, p < .001) but her boyfriend also had a significant negative response (r = -.13, p < .001). The clear takeaway is that the

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one with positive illusions tends to enjoy their misperception, however, their partner does not.

Multiple Regression Analyses

Two regressions are reported here: (a) the impact of predictors on Proximate RS, and (b) the impact of predictors on Distance RS. The dependent variable for both regressions is Couple RS (the mean of the men's RS and the woman's RS). All regressions use Stepwise method of variable selection with a p-to-enter of .05 unless otherwise noted.

***Proximate relationships using Couple RS as the DV*:** For Proximate relationships, eight variables entered the regression equation: $R(1, 366) = .841$, $R^2 = .707$, $p < .001$. Thus 70.7% of the variance in Proximate relationship's RS is accounted for by the predictors. Individual predictors follow, order based on magnitude of Beta values:

The greatest predictor of Couple RS for Proximate couples was their Emotional Regulation (β = .28), followed by their Emotional Engagement (β = .26), then, Family & Friend support (β = .21), less feeling of Loneliness for men (β = -.15), shared Activities (β = .13), the men's Positive Illusions (β = .08), the women's enjoyment of the Sexual Relationship (β = .08), and the number of shared Dates (β = .06).

Distance relationships using Couple RS as the DV: For Distance relationships, there was lower statistical power than for Proximate relationships (Note DF differences: 1, 366 vs. 1, 228), and the set of predictors was quite different. Eleven variables entered the regression equation: $R(1, 228) = .812$, $R^2 = .659$, $p < .001$. Thus 65.9% of the variance in Distance couple's RS is accounted for by the predictors. Individual predictors follow, order based on magnitude of Beta values:

The greatest predictor of Couple RS for Distance couples was their Emotional Engagement (β = .25), followed by the woman's rating of the Permanence (β = .21), then, their Emotional Regulation (β = .15), the men's level of self-Disclosure (β = .13), and Family & Friend Support (β = .13). Couples' RS was diminished by a longer relationship (β = -.13), and the woman's Codependence (β = -.10). Finally, the couples' RS was enhanced if the woman perceived her partner Accurately (β = -.10), the man was Nurturing (β = .10), had stronger Emotional Stability (β = .08, p = .08), and there was more Face-to-Face communication (β = .08, p = .08).

Of interest is that only three variables as predictors of Couple RS are shared by Proximate and Distance couples (β values that follow are Proximate then Distance): Emotional Engagement (βs = .26, .25), Emotional Regulation (βs = .28, .15), and Family & Friend Support (βs = .21, .13). Only for Emotional Engagement are the scores similar. Five of the Proximate predictors and eight of the Distance predictors are unshared. Structural equation modeling confirmed (and expanded on) discrepancies revealed in the regression analyses.

Structural Equation Modeling

Creating a structural model with the data set presented challenges. There were 32 predictor variables for Proximate relationships and 32 predictor variables for Distance relationships. The resulting models were so complex that, even though fit indices suggested an excellent model fit, they were almost impossible to interpret.

The answer involved choosing to use only "couple variables" in the analyses. Several of the variables were already coupled: Relationship Satisfaction was the mean of the men's and the women's RS. Other variables were either couple specific (AQP, Length of the relationship, shared Activities, PSC Compatibility), or were determined to be interactive (hence "gender-neutral") and already included the perspectives of both men and women (Emotional Engagement, Emotional Regulation). Other variables were coupled by averaging the crisscrossed values for men and women for each predictor. For instance, the variable "Emotional Stability" in the model would be the average emotional stability of both partners. Variables that were thus coupled included: Friend & Family Support, Strength of Identity, Accuracy of perception, Positive Illusions, Loneliness, Space

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from each other, rating the Permanence of the Relationship, enjoyment of their Sexual relationship, Nurturance, amount of self-Disclosure, Emotional Stability, and Codependence.

By thus simplifying the model, the number of variables was reduced from 32 to 18 (14 for the Distance model) and systematic differences between Proximate and Distance couples emerged that evaded us earlier. Essentially, the structural models considered "how shared personal qualities in the relationship impact each other and the primary dependent variable, couple RS."

The structural model for Proximate relationships: The sample size (N = 406 couples) is entirely adequate for structural equation modeling based on the Bentler and Chow criterion of at least a 5:1 ratio of participants to free parameters (Bentler & Chow, 1987). With 36 free parameters the Proximate model has an 11:1 ratio. For the final Proximate model fit indices include: χ^2 (34, N = 406) = 43.48, p = .13; the Root Mean Square Error of Approximation (RMSEA) was .027; the 90% CI ranged from 0 to .05; The Comparative Fit Index (CFI) was .993. All predictors were allowed to covary. These values indicate an excellent model fit (Hu & Bentler, 1999).

The Proximate model employs four dependent variables and 14 predictors—described in paragraphs that follow. The primary dependent variable is Couple RS; the other three dependent variables are Emotional Engagement, Emotional Regulation, and Family & Friend Support.

Couple RS: The predictors of Couple RS include Emotional Regulation (β = .34), Family & Friend Support (β = .22), Emotional Engagement (β = .19), shared Activities (β = .15), less Loneliness (β = -.15), and enjoyment of the Sexual relationship (β = .10). The residual for Couple RS (.324) indicates that 67.6% of the variance is explained by these six variables.

Emotional Regulation: The predictors of Emotional Regulation include better Emotional Engagement (β = .30), greater Accuracy of perception (β = -.24), less Codependence (β = -.24), more Nurturance (β = .20), a shorter relationship (β = -.17), more Separation (β = .14), more self-Disclosure (β = .14), higher Emotional Stability (β = .14), greater PSC Compatibility (β = .12), and more positive Illusions (β = .10). The residual for Emotional Regulation (.482) indicates that 51.8% of the variance is explained by these ten variables.

Emotional Engagement: The predictors of Emotional Engagement include better Friend & Family Support (β = .36), more Emotional Regulation (β = .30), greater rating of Permanence (β = .30), greater enjoyment of the Sexual relationship (β = .20), more self-Disclosure (β = .17), more shared Activities (β = .14), better Accuracy of perception (β = -.12), and greater strength of Identity (β = .08). The residual for Emotional Engagement (.378) indicates that 62.2% of the variance is explained by these eight variables.

Family & Friend Support: The predictors of Family & Friend support include better Emotional Engagement (β = .36), greater rating of Permanence (β = .22), less Loneliness (β = -.17), lower rating of Codependence (β = -.15), and more Nurturance (β = .09). The residual for Family & Friend support (.569) indicates that 43.1% of the variance is explained by these five variables.

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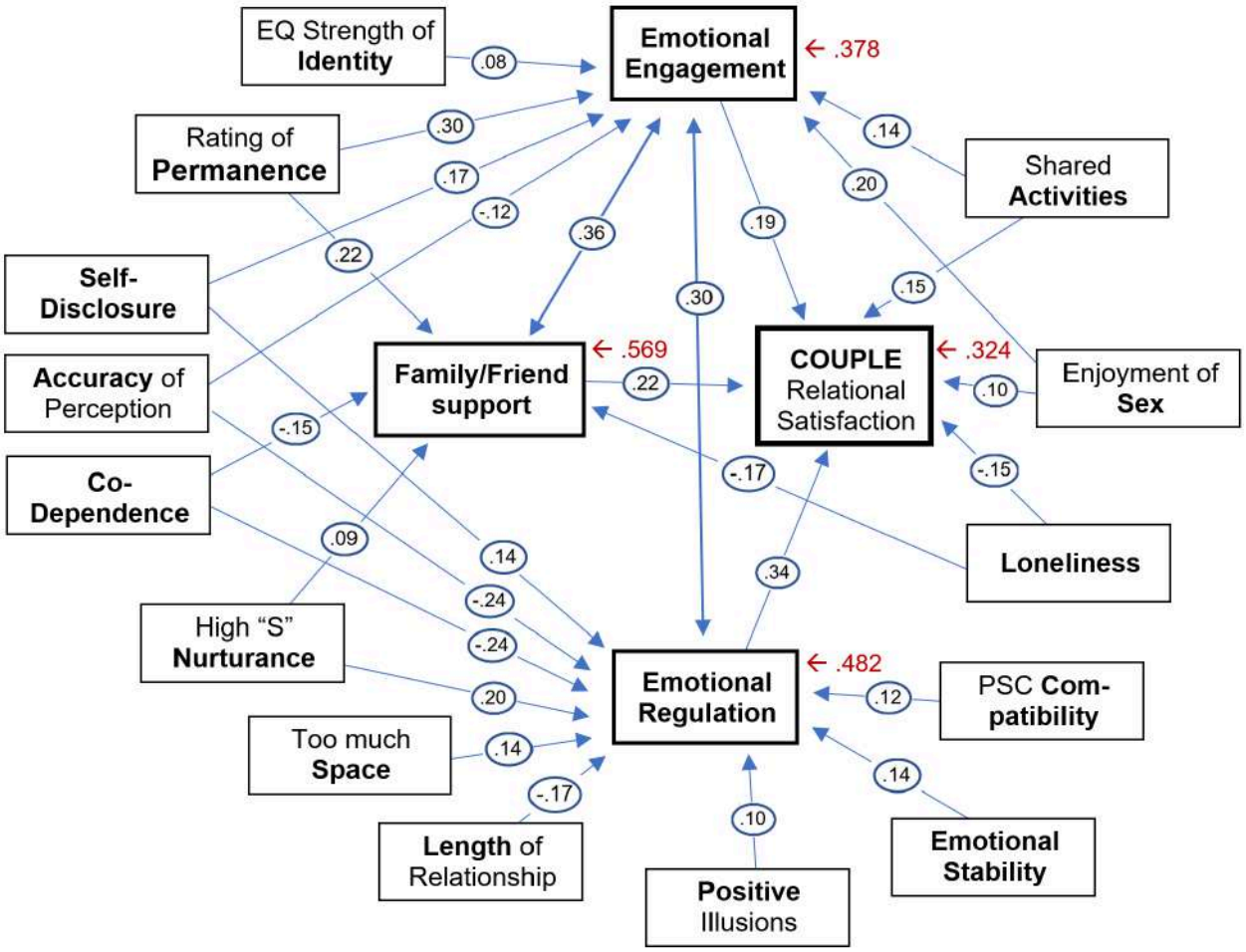

Figure 1: Displays the Proximate Structural Model

***The structural model for Distance relationships*:** The sample size (N = 237 couples) is adequate for structural equation modeling based on the Bentler and Chow criterion of at least a 5:1 ratio of participants to free parameters (Bentler & Chow, 1987). With 38 free parameters the Distance model has a 6:1 ratio. For the final Distance model fit indices include: χ^2 (16, N = 237) = 26.102, p = .053; the Root Mean Square Error of Approximation (RMSEA) was .055; the 90% CI ranged from 0 to .09; The Comparative Fit Index (CFI) was .984. All predictors were allowed to covary. These values indicate a good model fit (Hu & Bentler, 1999).

The Distance model employs four dependent variables and 10 predictors—described in the following paragraphs. As with the Proximate model, the primary dependent variable is Couple RS; the other three are Emotional Engagement, Emotional Regulation, and Family & Friend Support.

Couple RS: The predictors of Couple RS include Emotional Engagement (β = .27), greater rating of Permanence (β = .23), less Codependence (β = -.15), a shorter relationship (β = -.15), Emotional Regulation (β = .14), Family & Friend Support (β = .12), greater PSC Compatibility (β = .10), greater Emotional Stability (β = .09), more Nurturing (β = .08), more self-Disclosure (β = .08), and greater Accuracy of perception (β = -.06). The residual for Couple RS (.380) indicates that 62% of the variance is explained by these nine variables.

Emotional Regulation: The predictors of Emotional Regulation include greater Accuracy of perception (β = -.37), better Emotional Engagement (β = .25), more Nurturance (β = .24), a shorter relationship (β = -.20), more shared Activities (β = .07), and more positive Illusions (β = .04). The residual for Emotional Regulation (.614) indicates that 38.6% of the variance is explained by these seven variables.

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Emotional Engagement: The predictors of Emotional Engagement include greater rating of Permanence (β = .31), more shared Activities (β = .29), Emotional Regulation (β = .25), better Friend and Family support (β = .21), better Accuracy of perception (β = -.16), a shorter relationship (β = -.14), more Nurturance (β = .11), and more self-Disclosure (β = .09). The residual for Emotional Engagement (.335) indicates that 64.5% of the variance is explained by these eight variables.

Family & Friend Support: The predictors of Family & Friend support include better Emotional Engagement (β = .21), greater Permanence (β = .20), lower rating of Codependence (β = -.19), greater Accuracy of perception (β = -.16), more Nurturing (β = .15), and greater Emotional Stability (β = .09). The residual for Family & Friend support (.609) indicates that 39.1% of the variance is explained by these five variables.

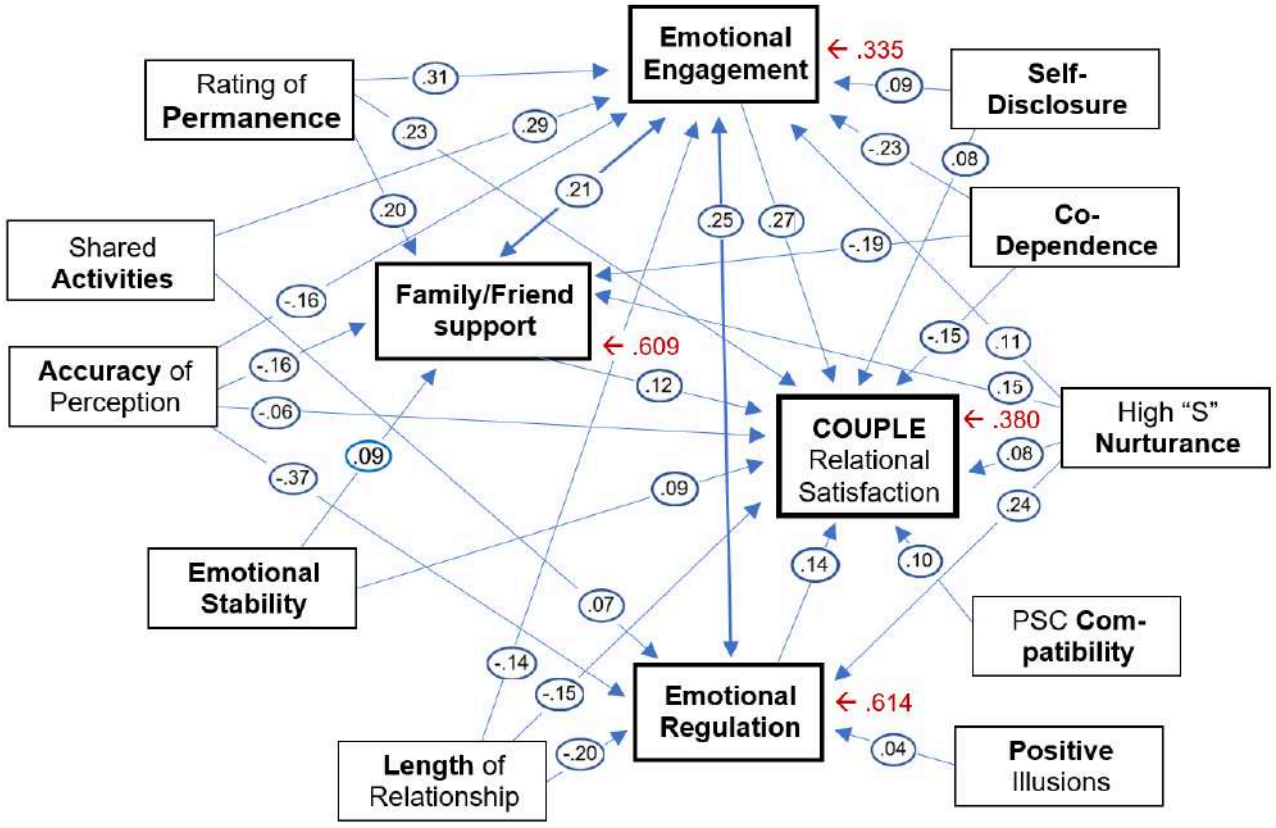

Figure 2: Displays the Distance structural model

Discussion

The discussion begins by a thorough assessment of relevant findings from the two structural models. This will be followed by additional findings from other analyses. We will conclude with key takeaways, limitations of the study, and avenues for future research.

Proximate-Distance Differences based on the Structural Model

The two structural models provide some systematic differences between Proximate and Distance relationships. To assist in clarity, in the discussion below, we will often include the beta weights as we discuss the relative impact of variables on each other. Since beta weights are partial correlations that exclude variance due to other variables in the model, those values can often be summed (there are some exceptions) to identify the relative impact of a particular variable in the model (see Zeiglari, 2017). We also often exclude the "β" as we identify beta weights. For instance: "Enjoyment of the Sexual Relationship predicted Couple RS (.10) and Emotional Engagement (.20)."

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Variables in the Proximate Model that were not in the Distance Model. Four variables played a role in the Proximate model that were not present in the Distance model. Strength of Identity is not discussed as the impact was minor. However, in the Proximate model three variables played a substantial role: (a) enjoyment of Sex [predicts higher Couple RS (.10) and greater Emotional Engagement (.20)]; (b) the impact of Loneliness [predicts lower Couple RS (-.15) and less Family & Friend support (-.17)]; and (c) the influence of distress due to too much Separation [predicts greater Emotional Regulation (.14)].

Sexuality: We deal with a smaller data set here as 20% of the couples reported that they were not sexually active. Goldsmith and Byers (2018) revealed that Distance couples need to be more innovative in sexual activity and experience sex less frequently. Sexual activity is present but, based on current findings, does not play as central a role in Emotional Engagement or Relationship Satisfaction as occurs with Proximate couples. One possible explanation is that while sexual activity (for Proximate couples) is associated with greater RS and Emotional Engagement, it is equally true that if the sexual relationship is going badly, it is just as strongly associated with lower RS and poorer Emotional Regulation (Lewandowski & Schrage, 2010; Smith, Lyons et al., 2011). For Distance couples, where sexual activity is less frequent due to distance, the ups and downs of the sexual relationship have less influence on Relationship Satisfaction of the couple. For Proximate couples, where the opportunity of sexual activity is higher, those same ups and downs have a greater impact on Couple RS.

Loneliness and Separation: Distance couples experience much higher loneliness than Proximate couples, but this represents the simple reality of not being together as much as they would like. Loneliness in a Proximate relationship (where daily contact is possible) suggests a relationship that is not satisfying or reveals personal flaws in the individual. The Separation variable measures the couples' sense of too much or too little time together [coded *too much time together* (1); *too much time apart* (7)]. Distance couples experience more space than they want—it is part of the dynamic of being distant. The positive correlation of Space with Emotional Regulation for Proximate couples suggests that their Emotional regulation is better if there is more time apart. With too much time together it is easier to get on each other's nerves and respond inappropriately.

Variables where the Dynamic is Similar: There are a number of variables and links between variables in which Proximate and Distance relationship are quite similar. Consult Figure 1 and Figure 2 for specific Beta values. (a) Codependence is an equal-opportunity destroyer with serious negative impact on Couple RS, Emotional Engagement, and Family & Friend support. (b) self-Disclosure is associated with greater Emotional Engagement, Emotional Regulation, and Couples RS. (c) Positive illusions have a limited but positive impact on Emotional Regulation in both models. (d) Emotional Stability is associated with Emotional Regulation and Friend & Family support. (e) Compatibility has a modest (but significant) effect on Emotional Regulation and Couple RS. (f) Shared Activities has a positive impact on Emotional Engagement, Emotional Regulation and Couple RS. And (g) both models have a strong bi-direction link between Emotional Engagement and Emotional Regulation (.30 for Proximate, .25 for Distance).

Length of the relationship: The length of the relationship has an almost equal negative impact for couples in either a Proximate or a Distance relationship. The common-sense explanation is that they may have moved beyond the "in love" phase and are beginning to experience less emotional intensity and have discovered that their partner is not "perfect". As the relationship develops and continues Emotional Regulation becomes increasingly important to deal with the inevitable stresses and irritations.

Emotional Engagement: Many studies show Emotional Engagement to be the greatest single predictor of Relationship Satisfaction-particularly among married couples (e.g., George, Anderson et al., 2023; Johnson, 2004). Emotional Engagement boasts more similarities than

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differences when comparing Proximate and Distance couples. For both, Emotional Regulation is a major predictor of Couple Relationship Satisfaction. The amount of variance explained by the predictors of Emotional Engagement is also similar, R^2 = .62 for Proximate; R^2 = .67 for Distance. The greatest single predictor of Couple RS (rating the Permanence or the relationship) is almost identical, βs = .31, .30. But there are differences (Distance value is listed first, then Proximate). Distance relationships show a greater negative impact of Codependence (βs = -.23, vs. -.06*ns*) and positive impact of Shared Activities (βs = .29, vs. .14); Proximate relationships show a greater impact of the support of Family & Friends (βs = .21, vs. .36).

Differences of Dynamics for Variables that Occur in Both Models: In addition to variables that occur in Proximate relationships but are absent in a Distance relationship, there are substantial differences in patterns of correlations between variables that occur in both models.

Accuracy of perception: Accuracy of perception is a major player in both models. For Proximate couples, Accuracy of perception affects two of the dependent variables: greater Emotional Engagement (-.12) and better Emotional Regulation (-.24). For Distance couples, Accuracy of perception plays a much larger role and impacts all four of the dependent variables: Greater Accuracy is associated with greater Emotional Engagement (-.16), more Family & Friend support (-.16), has a large impact on Emotional Regulation (-.37), and a direct impact on Couple RS (-.06). The total impact of Accuracy in Proximate RS (.36) is substantially less than that of Distance relationships (.75). Literature suggests that the greater discipline involved for Distance couples results in a more satisfying couple relationship. In this case, discipline may translate into greater efforts to view their partner more accurately.

Nurturance: A personal temperament that involves a nurturing relationship with a romantic partner plays a significant part in both models. For Proximate relationships, higher Nurturance is associated with greater Emotional Regulation (.20) and Family & Friend support (.09). For Distance couples, just like Accuracy of perception, Nurturance impacts all four dependent variables: A nurturing temperament is associated with greater Emotional Engagement (.11), more Emotional Regulation (.24), greater Family & Friend support (.15), and has a direct impact on Couple RS (.08). Once again, the impact of Nurturance is much greater in Distance Relationships (.58) than in Proximate Relationships (.29).

Emotional Regulation: More of the variance in Emotional Regulation is predicted in Proximate relationships (R^2 = .518) than in Distance relationships (R^2 = .386). Many factors impact Emotional Regulation in Proximate couples including greater Emotional Engagement (.30), higher Compatibility (.12), more Emotional Stability (.14), more Positive Illusions (.10), a shorter relationship (-.17), too much Space (.14), more Nurturing (.20), less Codependence (-.24), greater Accuracy of perception (-.24), and more self-Disclosure (.14). By contrast, Distance relationships find only five variables impacting Emotional Regulation: a shorter relationship (-.20), greater Accuracy of perception (-.37), more Shared Activities (.07), greater Emotional Engagement (.25), and more Nurturing (.24).

As alluded to earlier, Proximate relationships have more frequent face-to-face interaction that increases the likelihood of conflict or tension. Hence, both the impact of Emotional Regulation (on Couple RS) and the factors that contribute to Emotional Regulation are more prominent. Literature does not help us much here. Beckmeyer and colleagues (2021) and Cionea and colleagues (2019) indicate that not much difference is reported on conflict or serial arguments between Proximate and Distance couples.

Family & Friend support: The support of Family & Friends is more important for Proximate couples. First the link between Family & Friend support with Couple RS is .22 for Proximate Couples and only .12 for Distance couples. The strength of relationship between two predictors

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are substantially different (Proximate value first), including the impact of Emotional Engagement (βs = .36, vs. .21) and Accuracy of perception (βs = -.16 vs. -.05*ns*).

There is literature support for this perspective: Johnson and Hall (2021) reveal that Distance couples have a lower network of peer support and Holmes (2010) speaks of the likelihood of more abstract forms of support. It may be that Proximate couples are more likely to bring their romantic partner to visit their family and have greater ongoing interactions with friends.

T-test Differences, AQP, and Regressions

T-tests: The t-tests that compared Proximate with Distance couples gave the first glimpse of significant differences between the two types of relationships. Other than the axiomatic differences (less face-to-face time, more use of technology to communicate, lonelier, etc.) the t-tests lent support to Delatorre & Wagner's (2019) contention that because Distance couples required greater effort to maintain the relationships, a more positive profile emerges. T-test differences were rarely large (always < .05) but managed 100% indicating that Distance couples were healthier than Proximate couples, including (for both men and women in each setting): greater Relationship Satisfaction, longer relationships, greater Emotional Engagement, better Emotional Regulation, greater strength of Identity, higher Compatibility, greater rating or Permanence of the relationship, more Nurturing, more self-Disclosure and less Codependent.

AQP Acquaintance Potential: The hope that attended inclusion of this variable (derived from three qualitative variables in the questionnaire) was largely disappointed. The pattern of correlations was similar to correlations with length of the relationship across a number of variables. The actual correlates with AQP included greater likelihood of Permanence, lower levels of Codependence, more shared Activities, and greater Family & Friend support. Only the lower Codependence may have been considered interesting. Finally, AQP did not achieve significance in any of the regression equations or in either of the structural models. The non-impact of a new variable may be due to the typical two reasons: (a) poor construction of the variable or (b) simply that there really is no (or little) effect. The authors tilt toward the latter interpretation.

Regressions: The primary regressions, using Couple Satisfaction as the criterion variable (with all variables showing high bivariate correlations with Couple Satisfaction as predictors), were used primarily as a preliminary step in creating the structural models. For regression, we included separate variables for men and women for both Distance and Proximate relationships. Using the Stepwise procedure, significant differences began to emerge between the Proximate regressions and the Distance regressions. As stated earlier, the authors were unable to distinguish systematic trends based on those regressions. A number of other regressions were conducted, using some of the key predictors (Emotional Engagement, Emotional Regulation, Family & Friend Support) as dependent variables along with a series of partial correlations. But all of this was simply the prelude to creating the structural models.

Weaknesses, Strengths, and Summation

Weaknesses: A weakness of the study was that there were so many variables that the authors struggled with its sheer complexity. The coupling of men's and women's values (creating an average for each of the predictors in the structural models) resulted in loss of variation but was required to create a model that was interpretable. Another problem is that when there are so many variables the issue of linear dependency and inter-item collinearity becomes an increasing challenge. The amelioration of that criticism is that the authors were well aware of the challenge when crafting the research and worked to make sure there was a minimum of collinearity between the dependent variable, Relationship Satisfaction, and any of the predictors. Finally, the psychometric distortion of Relationship Satisfaction (for reasons described earlier in the paper) may at times compromise the validity of findings.

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Strengths of the study: The authors give themselves high marks on a large diverse sample that allowed valid comparisons between Proximate and Distance relationships. The crisscross procedure allowed for greater objectivity of responses and allowed creation of comparison variables, particularly Accuracy of perception, that helped distinguish between Proximate and Distance couples. Two other variables derived from crisscrossed values (compatibility and enhancement/diminishment) were significant predictors in the final model but not nearly at the level of Accuracy of perception. Finally, the two structural models not only achieved excellent model fits but were instructive of critical differences when comparing Proximate with Distance couples—something not revealed in earlier analyses.

Major takeaways when contrasting Proximate versus Distance Relationships: The broad strokes include: (a) Distance couples boast a healthier overall profile supporting theories that the greater effort required to maintain a Distance relationship results in healthier relationships; (b) Accuracy of perception plays a much larger role for Distance couples than for Proximate; (c) Nurturance follows a similar pattern with a greater impact for Distance couples; (d) Family & Friend Support plays a larger role in Proximate relationships; (e) Emotional Regulation plays a larger role for Proximate couples who (due to proximity) are required to deal more frequently with any couples' stresses and irritations; (f) Sex does not enter into the model as a predictor of Relationship Satisfaction for Distance couples; and (g) Loneliness, highly characteristic of Distance relationships, does not have a negative impact on Relational Success for Distance couples but significantly diminishes Relational Satisfaction for Proximate couples.

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Table 1: Psychometrics, Indicators, Computation, Alphas of Critical Variables

Variable	code	computation	indicators	mean	std. dev	skew	kurtosis	alpha
Couple Relationship Satisfaction	CS	Mean of indicators	Security, loved, joy, appreciated, trust, respect, activities, fun & laughter, satisfied with relationship, partner, needs fulfilled	6.48	.60	-1.83	3.33	.93
Emotional Engagement	GN	mean of indicators	Support growth, emotional needs, love languages, express feelings, affection, verbally express love	6.02	.663	-1.16	1.46	.86
Emotional Regulation skills	GN	mean of indicators	Patience, (un)critical, (few) conflicts, resolve conflicts, resolution perspective, look for the good, listen	5.51	.70	-.57	.12	.82
Family & Friends' support	CS	mean of indicators	family support, friends support	6.47	.72	-1.68	2.16	.74
Shared Activities	CS	mean of indicators	traditions, dates, stimulating conversation, shared projects, plan for future	5.47	.85	-.55	.07	.71
Accuracy of Perception	M	$\frac{1}{n}\sum \lvert woman\ self\ rate - man\ ra$	38 primary variables	1.06	.36	.59	1.04	--
Accuracy of Perception	W	$\frac{1}{n}\sum \lvert man\ self\ rate - woman\ ra$	38 primary variables	1.00	.36	.78	1.76	--
Enhancement	M	$\frac{1}{n}\sum man\ rate\ woman - woman$	33 valanced variables	-.10	.53	-.05	.87	--
Enhancement	W	$\frac{1}{n}\sum woman\ rate\ man - man\ rat$	33 valanced variables	-.04	.54	-.21	1.03	--
Compatibility	GN	PSC of men with women on essence qualities	13 essence qualities	r = .32	.33	-.37	-.39	--
Strength of Identity	M	$\frac{1}{n}\sum 13\ CC\ essence\ qualities)$	13 essence qualities	5.05	.60	-.25	.27	--
Strength of Identity	W			5.08	.60	-.36	.30	--
Loneliness	CS	CC measure	(M + W)/2	*2.95*	1.27	.39	-.46	--
Amount of Space	CS	CC measure	(M + W)/2	*4.51*	1.12	.43	-.29	--
Permanence	CS	CC measure	(M + W)/2	*6.29*	.96	-1.44	1.33	--
Enjoyment of Sex	CS	CC measure	(M + W)/2	*6.39*	.69	-1.29	1.43	--
Nurturance	CS	CC measure	(M + W)/2	*5.96*	.79	-.62	-.21	--
Disclosure	CS	CC measure	(M + W)/2	*5.61*	.96	-.59	.50	--
Emotional Stability	CS	CC measure	(M + W)/2	*4.83*	.93	-.13	-.37	--
Co-dependence	CS	CC measure	(M + W)/2	*2.94*	1.00	.39	-.30	--

Code: M = men, W = women, GN = gender neutral, CS = Couple specific, CC = criss-crossed

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