

The sex-specific associations between suicidality and post-traumatic stress disorder in patients with physical injuries

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To the editor:

Post-traumatic stress disorder (PTSD) arises after traumatic experiences, presenting with symptoms like reliving trauma, avoidance of reminders, mood changes and increased arousal, significantly affecting life quality and daily functioning.¹ A severe complication of PTSD is suicidality, notably contributing to the higher mortality among PTSD sufferers.² The complex relationship between PTSD and suicidality is well documented, yet its mechanisms are not fully understood. Understanding how early suicidality might signal the onset of PTSD is crucial for timely interventions.³

Current research often focuses on single-time PTSD assessments, conducted from 1 month to 2 years after trauma, missing the potential variability in PTSD symptoms over time.⁴ There is a lack of detailed study on how the link between PTSD and suicidality evolves, particularly considering the role of sex differences. Women report PTSD at rates two to three times higher than men, with about 10%–12% of women and 5%–6% of men affected in their lifetimes.⁵ This disparity is attributed to various psychosocial and biological factors.⁶ Similarly, sex differences in suicidality are significant, with women more prone to suicidal thoughts and attempts, influenced by a complex interplay of factors.

Given these intricacies, the interaction between PTSD and suicidality could vary significantly between men and women, suggesting different trajectories from trauma to PTSD and suicidality risk. This hypothesis underscores the importance of sex-specific approaches in research and intervention. Despite its relevance, this area remains largely uninvestigated, representing a critical gap in

the literature. This study aimed to explore the sex-specific dynamics between PTSD and suicidality over 2 years after trauma, analysing suicidality patterns immediately after trauma and their impact on PTSD progression by using data from a prospective study involving Korean patients who have experienced physical injuries.

STUDY OUTLINE

In this segment of the broader biomarker-based diagnostic algorithm for post-traumatic syndrome (BioPTS) study, aimed at advancing PTSD diagnostic models, we conducted a focused analysis on a subset of participants. Comprehensive details of the study design have been previously described in a design paper.⁷ These individuals, having sustained physical injuries, were part of the BioPTS enrolment between June 2015 and January 2021 at a trauma centre. Eligibility criteria are provided in online supplemental materials. Initial assessments were carried out within a month of hospital admission, including comprehensive psychiatric evaluations, socio-demographic data collection such as sex, clinical profile analysis and a detailed assessment of suicidality. The longitudinal nature of the study is underscored by successive PTSD assessments via structured telephone interviews at 3, 6, 12 and 24 months after injury.

BASELINE EVALUATIONS

Suicidality assessment

The Brief Psychiatric Rating Scale (BPRS)⁸ suicidality item score was used. This is structured to elicit the participant's thoughts and feelings about life and self-harm. Participants were asked a series of questions: 'Have you

felt that life wasn't worth living?'; 'Have you thought about harming or killing yourself?'; 'Have you felt tired of living or as though you would be better off dead?'; and 'Have you ever felt like ending it all?' Their responses were carefully recorded and evaluated. Responses were measured on a 7-point scale, ranging from 1 to 7, with higher scores indicating greater severity of suicidality. For the present analysis, the scoring was structured as follows: a score of 1 represented the absence of suicidal thoughts (not present), while scores ranging from 2 to 7 indicated varying degrees of suicidality (present).

Other baseline characteristics

A comprehensive evaluation of various sociodemographic and clinical characteristics was conducted at baseline, including age, sex and injury severity, as well as psychological assessments using established scales. These scales and characteristics aimed to capture a wide range of potential factors influencing PTSD development. Detailed descriptions are provided in online supplemental materials and online supplemental table S1.

FOLLOW-UP DIAGNOSIS OF PTSD

For diagnosing PTSD, this study employed the Clinician-Administered PTSD Scale (CAPS-5) based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria.⁹ The CAPS-5 was administered by two research nurses, who were specifically trained and supervised by experienced research psychiatrists, to ensure adherence to the standardised administration protocol. The training included detailed review sessions of the CAPS-5 manual, role-playing exercises and observation of administered assessments until proficiency was established. To establish a diagnosis, participants had to meet specific criteria across several symptom clusters: a minimum of one symptom from cluster B, one from cluster C, two from cluster D and one from cluster E, alongside fulfilling the requirements of clusters F and G. Recognised for its high reliability and validity, CAPS-5, even when administered via telephone, offers a robust framework for PTSD evaluation.¹⁰ The study defined the outcome variables as the presence of PTSD at each follow-up interval and the occurrence of any PTSD diagnosed at least once during the follow-up period.

The analysis included participants who underwent at least one evaluation after the initial baseline. This criterion aligns with the DSM-V guidelines,¹ which allow for PTSD diagnosis 1 month after trauma. We first compared groups with and without any PTSD during follow-up using t-tests for continuous variables and χ^2 tests for categorical variables. Variables significantly associated with PTSD ($p < 0.05$) were identified as covariates for subsequent analyses. The association of the BPRS suicidality item scores with sex was determined using t-tests. The relationships of suicidality and sex with any PTSD were initially examined using binary logistic regression before and after adjustment for the selected covariates. To explore

the potential modifying effects of sex on the relationships between suicidality and any PTSD, multinomial logistic regression was used after adjustment for the chosen covariates. The same analyses were repeated for each follow-up point to discern any sex-specific associations. All statistical tests were two sided, with a significance level set at 0.05. Statistical analyses were carried out using the SPSS V.21.0 software.

RECRUITMENT AND BASELINE CHARACTERISTICS

The recruitment process from the initial assessment to the 24-month follow-up and the prevalence of PTSD are depicted in online supplemental figure S1. Of the 1142 patients who met the eligibility criteria and agreed to participate, 95 (8.3%) discontinued participation before the 3-month evaluation, resulting in 1047 patients (91.7%) for the final analysis. Notably, baseline characteristics did not statistically differ between participants who remained and those who discontinued (all $p > 0.01$). Within the analysed sample, 122 patients (11.7%) were diagnosed with any PTSD at some point over 24 months. Descriptive statistics of baseline characteristics including assessment scales are presented in the first column of online supplemental table S1. Comparisons of baseline characteristics between patients with and without any PTSD are detailed in the second to fifth columns of online supplemental table S1. PTSD was significantly associated with age, education, cohabitation status, psychiatric history, exposure to previous traumatic events, childhood abuse and levels of anxiety and depression. These eight factors were used as covariates in the later adjusted analysis. The mean (SD) BPRS suicidal item scores were significantly higher in females (1.3 (0.7)) compared with males (1.2 (0.5)) ($p = 0.005$).

ASSOCIATIONS OF SUICIDALITY AND SEX WITH ANY PTSD

The results of binary logistic regression analyses on the associations of suicidality and sex with any PTSD are detailed in online supplemental table S2. Present suicidality at baseline and female sex were significantly associated with the occurrence of any PTSD. These significant associations persisted even after adjusting for the identified covariates.

MODIFYING THE EFFECTS OF SEX ON ASSOCIATIONS BETWEEN SUICIDALITY AND PTSD

The results of multinomial logistic regression to identify modifying effects after adjustment are graphically represented in figures 1 and 2. A notable sex-dependent variation in the association between suicidality and PTSD status emerged. Specifically, suicidality was significantly linked to PTSD in males but not in females, as indicated by significant interaction terms (figure 1 and online supplemental table S2). PTSD was diagnosed in 86 (8.2%) of 1047 participants at 3-month evaluation points, 73 (7.2%)

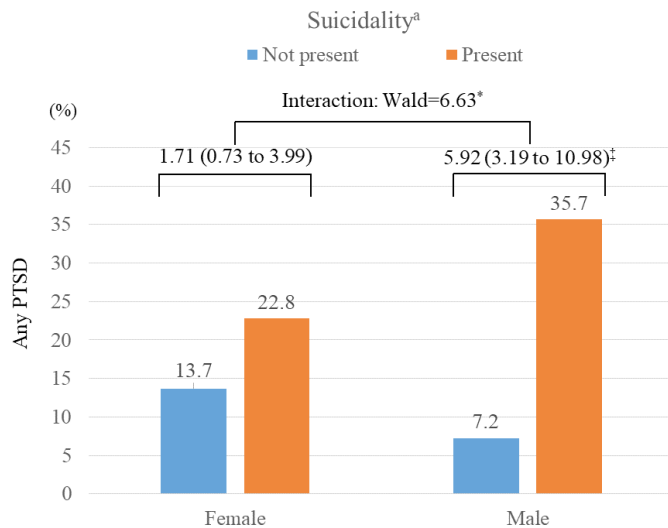


Figure 1 Modifying effects of sex on the associations of suicidality at baseline with any post-traumatic stress disorder (PTSD) over 2 years in 1047 patients with physical injuries. ORs (95% CIs) were calculated for not present versus present suicidality at baseline on the development of any PTSD over 2 years adjusted for age, education, living alone, previous psychiatric disorders, previous traumatic events, any childhood abuse and scores on Hospital Anxiety and Depression Scale-anxiety subscale and Hospital Anxiety and Depression Scale-depression subscale. ^aSuicidality was evaluated by the Brief Psychiatric Rating Scale suicidality item score ranging from 1 (not present) to 7 (extremely severe). * $p < 0.05$. [‡] $p < 0.001$.

of 1014 participants at 6-month evaluation points, 46 (4.7%) of 971 participants at 12-month evaluation points and 35 (3.8%) of 918 participants at 24-month evaluation points. Consistent with the overall findings, the relationship between suicidality and PTSD at each follow-up point remained significant solely in males with significant interaction terms (figure 2).

This 2-year longitudinal study in patients with physical injuries identified distinct sex-specific associations between suicidality and PTSD, notably revealing significant correlations in males. This correlation was consistent across all follow-up points (3, 6, 12 and 24 months), highlighting the importance of early suicidality in predicting PTSD, particularly in men.

Prior research has not systematically examined the sex differences in the predictive role of suicidality for PTSD in relation to the nature of traumatic events. This notable gap in the existing literature underscores the importance of our study, which is the inaugural exploration of these dynamics specifically within the context of patients who have experienced physical injury trauma. While focusing on this distinct group may somewhat limit the immediate generalisability of our findings, it crucially lays the groundwork for future research into how different types of traumas impact the complex interplay between suicidality and PTSD. Our study, therefore, provides pivotal initial insights and emphasises the need for comprehensive investigations across varied trauma contexts.

Several explanations are possible for the observed sex-specific associations. A primary consideration is the difference in help-seeking behaviour between the sexes. It is well documented that women are more likely to seek help for psychological problems, including suicidal ideation, often consulting general practitioners.^{5 6} In contrast, men may be more inclined to conceal their psychological struggles and less likely to seek professional help.¹¹ This disparity in health-seeking behaviours could lead to differences in the reported incidence and diagnosis of PTSD. Second, research indicated that biological and neurological differences between sexes can influence the development and manifestation of PTSD and suicidality. Hormonal differences, particularly those involving oestrogen and testosterone, may affect how stress and trauma are processed in the brain. For instance, oestrogen has been linked to higher rates of PTSD in women due to its influence on the brain's fear and stress response systems.¹² Third, societal norms and expectations about gender roles can significantly impact how individuals experience and express distress. Men, for instance, may feel societal pressure to appear strong and unemotional, leading them to under-report symptoms of PTSD and suicidality.¹³ This could partly explain why the association between suicidality and PTSD is observed more in men, as they might only express these symptoms when they are particularly severe.

The limitations of this study include the recruitment of participants exclusively from a single trauma centre, which, while beneficial for consistency in evaluation and follow-up, may limit the generalisability of the results. Suicidality was assessed with the BPRS item, effective for evaluating ideation and behaviour severity.¹⁴ However, this single item might not fully capture the complexity of suicidal thoughts and behaviours. Although follow-up evaluations were conducted via telephone interviews, a method shown to be as valid as face-to-face interviews in previous research,¹⁰ it is essential to consider the potential limitations of this approach.

A major strength of our study was the methodical recruitment of all eligible patients who had recently experienced physical injuries, minimising selection bias and ensuring a representative sample. We employed a structured research protocol with frequent follow-up assessments to mitigate bias from variable examination times. Consistency and reliability were further ensured by using standardised scales like the CAPS-5 for PTSD diagnosis. Additionally, we collected a wide range of covariates at baseline, and our long-term follow-up showed no evidence of selective attrition, bolstering the study's robustness.

In conclusion, this study provides significant insights into the sex-specific associations between suicidality and PTSD following physical injuries, emphasising the crucial role of gender in PTSD development. Our results advocate for gender-sensitive public health strategies to prevent PTSD and suicidality and call for clinicians to tailor treatments to the distinct experiences of men and women. Highlighting the need for early, comprehensive suicidality

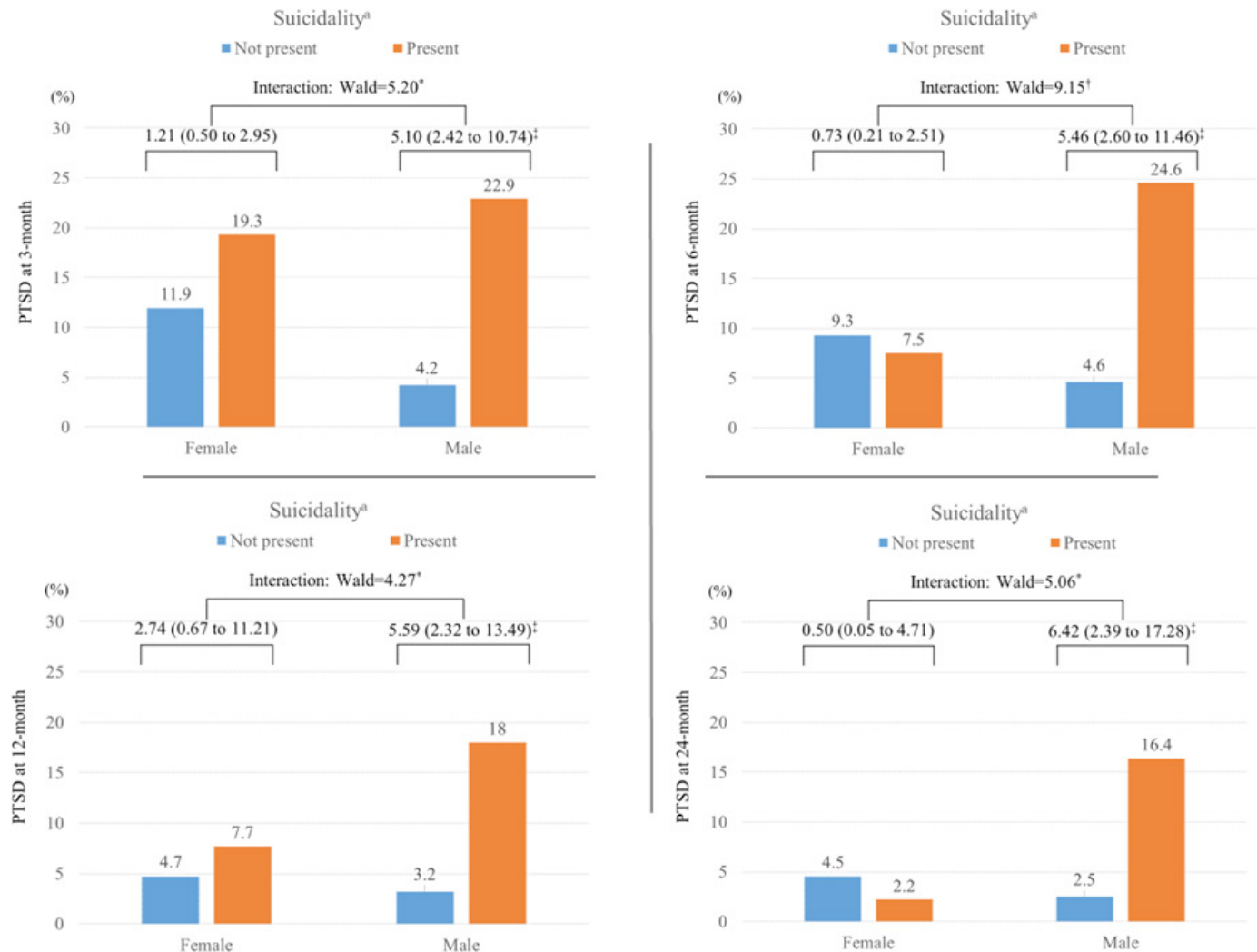


Figure 2 Modifying effects of sex on the associations of suicidality at baseline with post-traumatic stress disorder (PTSD) at 3, 6, 12 and 24 months in patients with physical injuries. ORs (95% CIs) were calculated for not present versus present suicidality at baseline on the development of any PTSD over 2 years adjusted for age, education, living alone, previous psychiatric disorders, previous traumatic events, any childhood abuse and scores on Hospital Anxiety and Depression Scale-anxiety subscale and Hospital Anxiety and Depression Scale-depression subscale. ^aSuicidality was evaluated by the Brief Psychiatric Rating Scale suicidality item score ranging from 1 (not present) to 7 (extremely severe). * $p < 0.05$. † $p < 0.01$. ‡ $p < 0.001$.

screening, this study points towards the necessity of timely mental health interventions. Future research should expand to multicentre studies and various trauma types. Moreover, investigating the relationships between fluctuations in suicidality over time and PTSD is worthwhile. Such inquiries are vital for advancing our understanding of these complex relationships, ultimately guiding more effective prevention and treatment methods.

Contributors J-MK and I-SS designed the study. H-JK and J-WK constructed and performed the study methodology. J-MK and S-WK contributed to project administration. J-CK, S-WK and I-SS contributed to validation. J-MK, J-WK, H-JK and HJ acquired data and curated the data. J-MK, J-WK and H-JK contributed to formal analysis. J-MK contributed to writing the original draft. J-MK, H-JK, J-WK, BJC and J-YL contributed to reviewing and editing the draft.

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Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s)

Ethics approval This study involved human participants and was approved by CNUH IRB (approval number: CNUH 2015-148). Participants gave informed consent to participate in the study before taking part.

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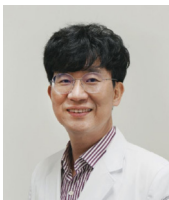
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