

Factors Associated with In-hospital Mortality in Severe Burn Patients in Songklanagarind Hospital: A Retrospective Study

Atthawit Mongkornwong, M.D.¹, Rassamee Sangthong, M.D., Ph.D.²,
Thara Tunthanathip, M.D., Ph.D.¹, Surasak Sangkhathat, M.D., Ph.D.¹

¹Division of Plastic and Reconstructive Surgery, Department of Surgery, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

²Department of Epidemiology, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.

Received 3 February 2020 • Revised 17 July 2020 • Accepted 30 July 2020 • Published online 18 November 2020

Abstract:

Objective: This study aimed to analyze the factors associated with mortality in burn patients in order to develop a nomogram for predicting mortality that can be used as a guideline to treat major burn patients.

Material and Methods: This was a retrospective study done in Songklanagarind Hospital, Hat Yai, Songkhla, Thailand. The study included major burn patients who were admitted to the burn unit or the intensive care unit between the years 2011 and 2018, and analyzed demographic data and significant factors associated with mortality.

Results: A total of 127 major burn patients were treated during the study years, with a mean age of 33 years with an average total burn surface area (TBSA) of 43.5%. The most common cause of the burns was flame injury, and the most significant factors associated with mortality were TBSA >55.0%, blood creatinine >1.2 milligrams per deciliter (mg/dL) and face involvement.

Conclusion: The 3 significant burn-related factors of TBSA >55.0%, blood creatinine >1.2 mg/dL and face involvement can be used to predict mortality using the nomogram created in this study.

Keywords: low-to-middle-income countries, major burn patients, mortality, nomogram

Contact: Atthawit Mongkornwong, M.D.
Division of Plastic and Reconstructive Surgery, Department of Surgery, Faculty of Medicine,
Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
E-mail: Atthawit_sx@hotmail.com

J Health Sci Med Res 2021;39(3):191–200
doi: 10.31584/jhsmr.2020775
www.jhsmr.org

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Introduction

Burn and fire injuries are among public health concerns worldwide, especially in low-and-middle-income countries where fire prevention remains substandard. In 2014, statistics from the United States (US) showed that death from fire and burn injuries occurred to 3,194 people or at an estimated incidence of 1/100,000 population. Thermal injuries represent 1.3% of all injuries and the problem accounts for 1.6% of all trauma-related fatalities. When the mortality figures from burn injuries were analyzed with the 408,945 non-fatal burns reported in the US in the same year, burn-related deaths were about 0.8%.¹ According to the American Burn Association, approximately 40,000 hospitalizations in the US in the year 2016 was related to burn conditions and, among these, 3/4s were admitted to a burn center. In addition to the preceding data, the trend line reported by the web-based injury statistics query and reporting system governed by the US Centers for Disease Control and Prevention showed that the total number of burn patients was decreasing in general, but increasing in elderly population.² Considering the global incidence of fire and burn injuries, South East Asia was the area with the highest mortality rate from flame burn injuries with an incidence of 11.6 per 100,000 population.³

There are various causes of burn injury in patients admitted to burn centers. Flame burn is the predominant cause, followed by scald burn, heat contact, and electrical and chemical burns. Although the majority of incidences occur at home, burn injuries can also occur at work or on the street. A study from Iran reported that 60.0% of burns were accidental while most of the rest was occupational injuries.⁴ The age groups at high risk for burn injury are children under four years of age and the elderly more than 60 years of age. Management of severe burns requires intensive care from the scene to the burn center and usually involves high-cost treatment. It costs about

US \$1,000 per patient per day to provide adequate burn care in the developed world. Nevertheless, mortality in burn patients in these resource-competent countries was reported as high as 3.3%.⁵

In resource-limited countries, the mortality of severe burn patients is very high. A study from Iran reported an overall probability of death of 26.0%⁴ while a study from Pakistan reported 41.0% mortality.³ It has been estimated that more than 90.0% of burn-related deaths currently occur in low and middle income countries.⁶ The depth and extent of the burn are the most crucial factors associated with mortality. However, death can occur in severe burn patients not only from the acute physiologic insults caused by the burn itself, but may occur later during the admission due to hospital-acquired infections such as pneumonia or wound infection. Additionally we can use clinical and laboratory factors to predict mortality in burn patients and adjust our treatment plan accordingly. Suicidal attempt, female gender, extreme age⁷, and also co-morbidities and complications have been associated with increased mortality risk.⁵

Songklanagarind Hospital is a level-1 trauma center with a burn center situated in the southern part of Thailand. The burn center receives approximately 3-5 severe burn patients per month from the surrounding hospitals. A rough figure of in-hospital mortality of burn patients in our center is 10.0%. In this study, we aimed to examine the characteristics of severe burn patients in our service, beginning with quantitation of the exact number of in-hospital mortalities, and we also analyzed the factors associated with in-hospital mortality in these cases. The causes of injury, intensive care requirement, ventilator days, length of hospital stay, in-hospital expenditures and functional status after discharge were studied. It was expected that findings from the study would be useful in improving our care of burn patients.

Material and Methods

The study was approved by the Human Research Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC number 62-329-10-1). A retrospective study was conducted in the Department of Surgery at Songklanagarind Hospital. The study included major burn patients who were admitted to the burn unit or the intensive care unit between the years 2011 and 2018. Data collection began on the first day of admission and during the hospital course until discharge or death. Demographic data, admission laboratories, total body surface area injured from the burn, area or areas of injury, length of stay, wound dressing material, and nutrition supplements were recorded. The total burn surface area (TBSA) in terms of % total body surface area was calculated from the Lunde and Browder chart.¹ A severe burn was defined as TBSA >20.0%. More than 90.0% of the severe burn patients were initially admitted to the burn unit. Fluid resuscitation used a modified Parkland formula protocol, with a central venous catheter placed in either the subclavian or the femoral vein during the initial resuscitation phase. Microbiological studies including blood cultures or burn wound cultures were performed when there were clinical indications. In-hospital mortality was defined as death occurring during the admission, regardless of the cause of death. In order to analyze for factors associated with survival, parameters from the survival group were compared with those of the non-survivor group.

All values are expressed as median and standard deviation or as percentages, with each variable tested for differences between the survivor and non-survivor groups by univariate statistical methods (chi-squared test or Fisher's exact test) with significance accepted at p -value <0.05, and all significant variables by univariate analysis then included in multivariate analysis. Stepwise logistic-regression analysis was performed with selected predictive

factors for death. This analysis resulted in the final predictive model.

A nomogram was then constructed from the three statistically significant factors using the method proposed by Zang et al.⁸ The data set was separated into two parts at the proportion of 3:7. 30.0% of the data was used to perform an internal validation of the nomogram. The nomogram's sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated for death at various cut-off points of the total scores. The highest performance nomogram with optimal cut-off points was selected based on a Receiver Operating characteristic curve (ROC) and the area under the ROC was plotted. For interpretation of the ROC, area under the curve (AUC) values of ≥ 0.90 "excellent," ≥ 0.80 "good," ≥ 0.70 "fair," and < 0.70 "poor" were used. The statistical analysis was performed using R version 3.4.0 software (R Foundation, Vienna, Austria).

Results

Of 245 major burn patients admitted to our hospital during the study period, 127 were classified as severe burns and were included in this study. The baseline characteristics of the 127 severe burn patients are presented in Table 1. Eighty-eight patients were male, the mean age of the 127 patients was 33 years (range 21–43 years) and the mean TBSA was 42.5% (range 25.5–53.0%). Eighty patients (63.0%) had flame injury, 22 patients (17.3%) had electrical injury, 16 patients (12.6%) had scald injury and 9 patients (7.1%) had chemical injury. The mean length of stay was 68 days (range 13–86 days). Twenty-four patients (19.0%) died during their stay in the hospital and the median time to death in this group was 14.5 days (range 6–53.2 days). All patients with severe infection had positive blood culture. The most common pathogens in both groups were *Pseudomonas aeruginosa* and *Acinetobacter baumannii*. We also found drug-resistant

Table 1 Demographic and clinical data of study severe burn patients

Parameter	Frequency (%)	Median	Percentile 25–Percentile 75
Sex			
Male	88 (69.3)		
Female	39 (30.7)		
Age (years)		31	21.00–43.00
0–32	59 (46.5)		
>32	68 (53.5)		
Weight (kg)		60	55.00–65.00
Body mass index (kg/m ²)		22.2	18.63–25.63
Underlying disease			
Diabetes mellitus	2 (1.6)		
Hypertension	7 (5.5)		
Dyslipidemia	4 (3.2)		
Others	5 (3.9)		
Associated injury			
Head injury	7 (5.5)		
Maxillofacial injury	1 (0.8)		
Torso injury	4 (3.2)		
Limb fracture	2 (1.6)		
Initial laboratory values			
Hemoglobin (g/dL)		14.1	12.00–16.30
Leukocytes (cells/mm ³)		12,080	8,475–19,162
Platelets (10 ³ cells/cu.mm.)		227.5	193.00–357.00
Creatinine		0.91	0.64–1.08
Serum albumin (g/dL)		2.65	2.00–3.20
Burn area (%TBSA)		40	25.50–53.00
Number of operations (times)			
0–3	37 (31.4)		
4–5	81 (68.6)		
>5	9 (7.1)		
Time to first skin graft		34	21.00–57.00
Length of hospital stay (days)		45	13.00–86.50

kg/m²=kilogram per square meter, g/dL=gram per deciliter, mm³=cubic millimeter, cu.mm.=microliter, TBSA=total body surface area

microbes, most commonly *methicillin-resistant Staphylococcus aureus*. In cases with infection, the major causes of death were burn wound sepsis and ventilator-associated pneumonia. The main causes of death in patients without infection were pulmonary- and cardiac-related causes.

A comparison between the survival and non-survival groups is shown in Table 2. On univariate analysis, factors associated with in-hospital mortality included age

more than 32 years, TBSA more than 55.0%, facial involvement, hemoglobin of less than 9 g/dL, creatinine of more than 1.2 mg/dL, delayed feeding initiation and receiving blood transfusion (Table 3). Stepwise logistic regression showed three factors independently associated with mortality, including TBSA, high creatinine and facial involvement (Table 4).

Table 2 Comparisons between survival and mortality groups

Parameter	Number (%)	Survival cases	Mortality cases	p-value
All	127 (100.0)	103 (81.1)	24 (18.9)	
Age (years)				
0-32	59 (46.4)	57 (55.3)	2 (8.3)	<0.001
>32	68 (53.5)	46 (44.7)	22 (91.7)	
Sex				
Female	39 (30.7)	29 (28.2)	10 (41.7)	0.300
Male	88 (62.3)	74 (71.8)	14 (58.3)	
Body mass index (kg/m ²)				
<23.9	30 (60.0)	26 (63.4)	4 (44.4)	0.450*
>23.9	20 (40.0)	15 (36.6)	5 (55.6)	
Associated injury				
Present	13 (10.2)	10 (9.7)	3 (12.5)	0.710*
Absent	114 (89.8)	93 (90.3)	21 (87.5)	
Burn area (%TBSA)				
0.0-55.0	103 (81.1)	91 (88.3)	6 (25.0)	<0.010
>55.0	24 (18.9)	12 (11.7)	18 (75.0)	
Burn site**				
Face	58 (45.7)	37 (35.9)	21 (87.5)	<0.010*
Trunk	96 (75.6)	74 (71.8)	22 (97.1)	
Extremities	120 (94.5)	97 (94.2)	23 (95.8)	1.000
Hemoglobin (g/dL)				
0-9	12 (9.5)	7 (6.8)	5 (21.7)	0.040
>9	114 (90.5)	96 (93.2)	18 (78.3)	
Serum creatinine (mg/dL)				
0-1.2	106 (84.8)	92 (90.2)	14 (60.9)	0.020
>1.2	19 (15.2)	10 (9.8)	9 (39.1)	
Serum albumin (g/dL)				
0-3.5	84 (80.8)	65 (80.2)	19 (82.6)	1.000
>3.5	20 (19.2)	16 (19.8)	4 (17.4)	
Escharotomy				
No	114 (89.8)	95 (92.2)	19 (79.2)	0.070*
Yes	13 (10.2)	8 (7.8)	5 (20.8)	
Early feeding				
No	10 (7.9)	4 (3.9)	6 (25)	<0.003*
Yes	117 (92.1)	99 (96.1)	18 (75)	
Blood transfusion				
No	64 (50.4)	57 (55.3)	7 (29.2)	0.037
Yes	63 (49.6)	46 (44.7)	17 (70.8)	

*Fisher's exact test, **Some patients had more than 1 sites

kg/m²=kilogram per square meter, TBSA=total body surface area, g/dL=gram per deciliter, mg/dL=milligram per deciliter

Table 3 Univariate logistic regression analysis

Parameter	Odds ratio	95% CI
Age >32 years	13.63	3.05–61.01
Burn area >55.0%TBSA	22.75	7.55–68.53
Face involvement	12.49	3.49–44.68
Trunk involvement	4.31	0.95–19.51
Hemoglobin <9 g/dL	3.81	1.09–13.34
Creatinine >1.2 mg/dL	5.91	2.05–17.10
Early feeding	8.25	2.11–32.18
Blood transfusion	3.01	1.15–7.88

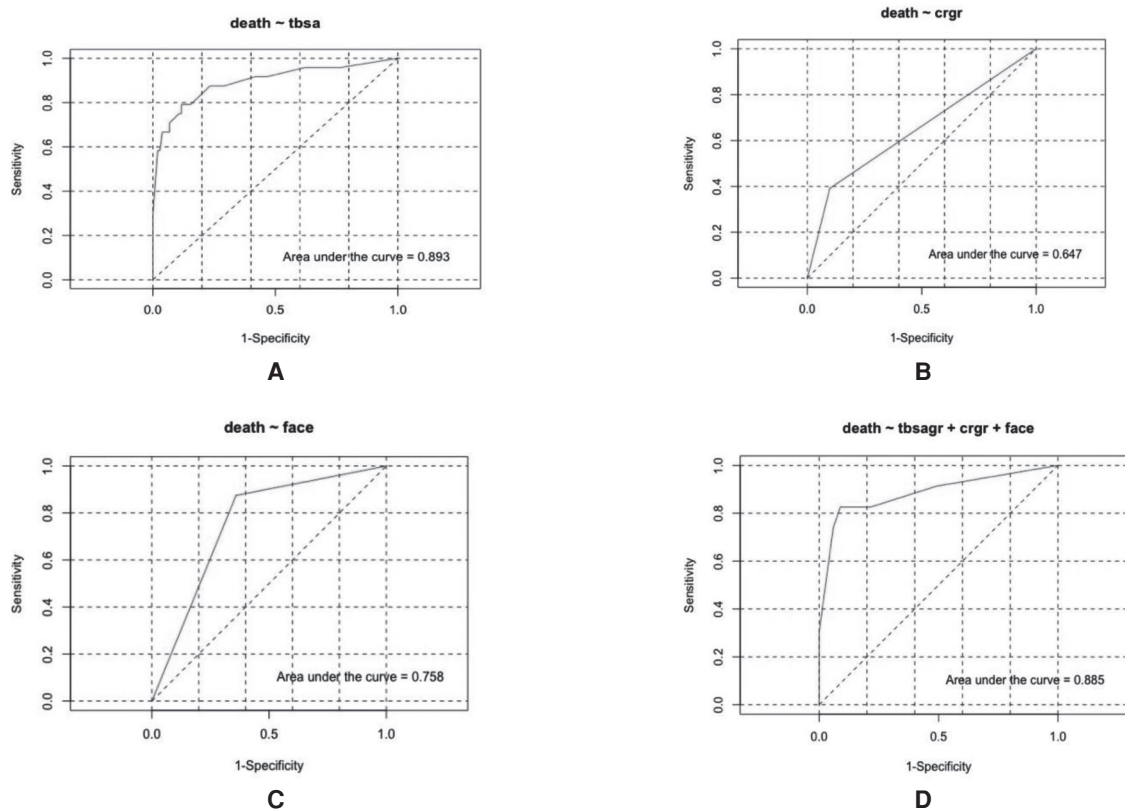
CI=confidence interval, TBSA=total body surface area, mg/dL= milligram per deciliter, g/dL=gram per deciliter

Table 4 Stepwise logistic regression (final model)

Parameter	Odds ratio	95% CI
Burn area >55.0%TBSA	10.28	1.00–105.35
Creatinine >1.2 mg/dL	13.53	1.20–152.03
Face involvement	15.28	1.23–190.14

CI=confidence interval, TBSA=total body surface area, mg/dL= milligram per deciliter

On an ROC curve plot between TBSA and probability of mortality, the AUC was 0.89 (Figure 1A). When we used a TBSA cut-off of 55.0%, the sensitivity was 11.6% and the specificity 75.0%, with a calculated lethal area

**Figure 1** The receiver operating characteristic curve plots of burn area, blood creatinine, face involvement and probability of mortality

fifty percent (LA50) of 76.0% of TBSA. Serum creatinine had prediction performance in the AUC of 0.647 (Figure 1B). Patients who had blood creatinine more than 1.2 mg/dL had increased mortality with sensitivity of 39.0% and specificity of 98.0%. Patients with face involvement had increased mortality with sensitivity of 35.9% and specificity of 87.5%, with an AUC of 0.76 (Figure 1C). On combining together the three significant factors, the AUC was 0.89 (Figure 1D).

The three significant factors were used to construct a nomogram with an aim to enable the physician to predict mortality (Figure 3). This nomogram predicted the probability of death using a TBSA >55.0%, face involvement and blood creatinine more than 1.2 mg/dL. Using a cutoff score of 114, this nomogram scoring system had an ROC-AUC of 0.84.

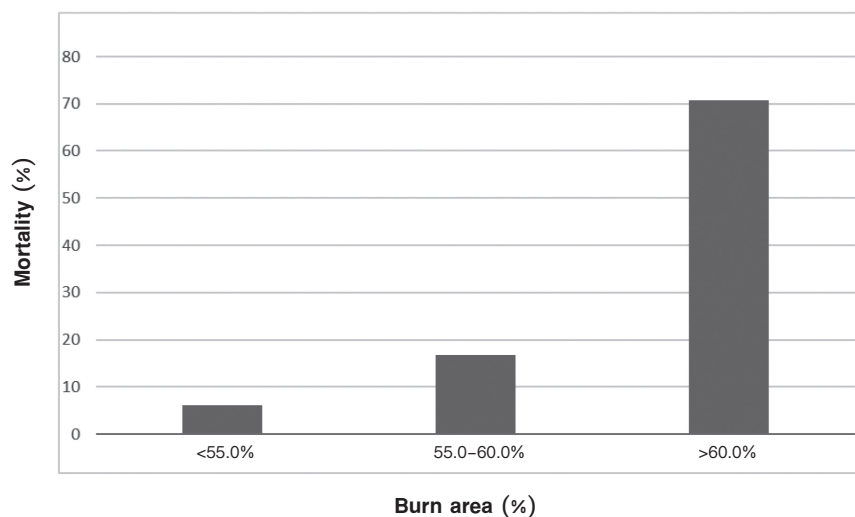
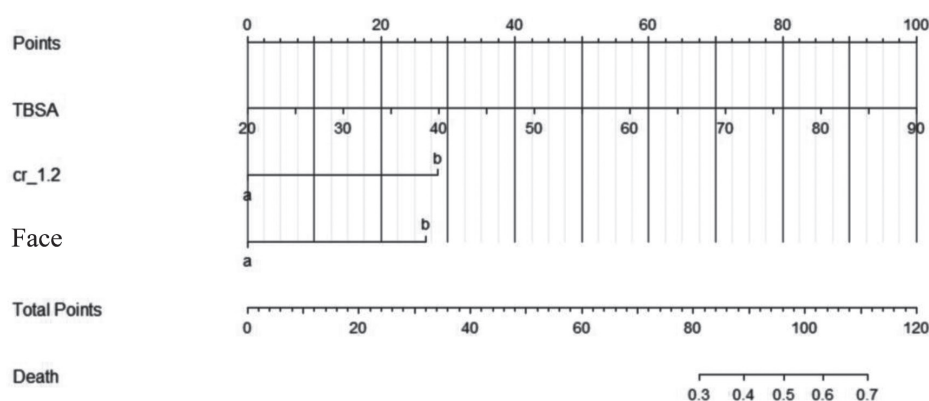


Figure 2 Bar chart showing the association between mortality and extent of burn area



TBSA=total body surface area

Figure 3 Nomogram to predict mortality in severe burn patients

Discussion

Patients with severe burn injury have a high chance of in-hospital mortality due to various reasons, both direct thermal injuries to vital organs and complications occurring during the treatment process. Some of these complications are preventable by improving the care process. A recent study from the Netherlands found a reduction in major burn mortality from 23.0% during the years 1987–1996 to 7.0% during the years 2007–2016.^{9,10} A study from Canada in which 15.0% overall mortality was reported emphasized that multi-organ failure and infectious complications were the two most common causes of death in major burn patients.⁹ The mortality rate of 20.0% in our severe burn patients in 10 years and it was higher than reports from developed countries.¹¹ However, our figure was comparable with other reports from developing countries, where flame burn remains a cause of major trauma-related fatalities.^{3,12,13} Consistent with all previous studies, TBSA was the most influential factor determining outcome in burn patients.^{14,15} Our study also found that the average LA50 of our patients was 76.0% of TBSA, which was comparable with other studies from southern Iran which found the LA50 was 66.5% of TBSA.^{16,17}

Effective initial resuscitation, including airway management and circulatory system restoration, is the crucial factor for survival in burn patients. Among the 24 mortality cases in our series, 5 (20.0%) occurred within five days and 12 (50.0%) occurred within 14 days of admission. All 12 cases with mortality within the first 14 days had TBSA >40.0% and 11 cases had facial involvement. Taken together with our finding that high serum creatinine was associated with unfavorable outcomes, the evidence suggests that management of circulatory failure and special attention to inhalation injuries should be priorities in improving the care process. As burns involving the facial area are associated with higher risk of inhalation injury^{18–20}, airway and respiratory care should

be promptly provided in patients with facial burns no matter how extensive the TBSA is.^{21,22} Early bronchoscopy in order to grade the severity of inhalation injury is advisable for cases with suggestive evidence such as signs of airway edema, respiratory failure, carboxyhemoglobinemia and adult respiratory distress syndrome. An association between high serum creatinine on arrival and in-hospital mortality in our series indicates that hypoperfusion is also an issue that needs further attention. Early provision of fluid resuscitation has been advocated as the most pertinent care in the initial phase of burn management.¹ Although prehospital care is available in major cities in Thailand, secure venous access and large volume resuscitation are frequently not successful, especially in cases with extensive burns involving one or more extremities. The issues of under-resuscitation and inhalation injury have also been addressed in burn case series from other south Asian countries.^{3,23} Future research should focus on how and how much fluid should be initiated at accident scenes and during transportation to the emergency department.

On univariate analysis, our study found that factors other than TBSA, facial involvement and high serum creatinine were associated with in-hospital mortality including age, anemia, and requirement of blood transfusion and delayed enteral feeding. Although these factors were statistically regarded as co-variate on multivariate analysis, they should not be overlooked. Anemia in burn patients can be a result of continuing blood loss from wounds and poorer blood cell production secondary to nutritional deprivation and septicemia. Early enteral feeding has been suggested by recent studies as a strategy which might ameliorate gut bacterial translocation and sepsis.¹¹ Elderly age has also been reported by various studies to be a determinant of adverse outcomes.¹² In our study, we found the cutoff age that gave different survival outcomes was around 35 years. This might be explained by the fact

that we seldom have burn cases in the elderly. Another explanation could be that young patients have more physiologic reserves and fare better through the treatment process.

Concerning the three factors independently associated with adverse outcomes in our patients, TBSA, facial involvement and high serum creatinine on admission, we found that a nomogram constructed based on the combination of these three factors had good performance in predicting in-hospital mortality in our patients. This nomogram could help in the future in calculating survival probability using these three parameters as inputs. The aim of using this nomogram is to quickly categorize burn patients into those with high risk and thus requiring more intensive resuscitation and invasive monitoring. In our setting, such high-risk patients should be immediately taken to the intensive care unit and provided with intensive physiologic support.

Conclusion

This study reviewed survival outcomes of severe burn patients in a tertiary setting in southern Thailand and found that the extent of injury, facial involvement and azotemia on admission were three factors independently related to in-hospital mortality. These parameters were used to construct a nomogram that predicts high-risk cases.

Conflicts of interest

All authors declare no personal or professional conflicts of interest

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