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Association of preoperative blood biomarkers with postoperative major adverse cardiac events and mortality in major orthopaedic surgery: a systematic review and meta-analysis

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ABSTRACT

Objective The association between preoperative blood biomarkers and major adverse cardiac events (MACEs) as well as mortality after major orthopaedic surgery remains unclear. This study aimed to assess the association between preoperative blood biomarkers and postoperative MACEs as well as all-cause mortality in patients undergoing major orthopaedic surgery.

Design A systematic review and meta-analysis.

Data sources PubMed, EMBASE, the Cochrane Controlled Trials Register and Cochrane Database of Systematic Reviews from inception to 20 October 2024 were searched.

Eligibility criteria Observational or experimental studies reporting the correlation between preoperative blood biomarkers and postoperative MACEs—categorised as short-term (within 3 months) or long-term (beyond 3 months)—and all-cause mortality in patients undergoing major orthopaedic surgery.

Data extraction and synthesis Data from studies reporting OR or HR and its 95% CI were pooled for analysis using random-effects model.

Results 21 preoperative blood-based biomarkers from 80 studies with 226 468 patients were analysed. Elevated preoperative cardiac biomarkers were correlated with a heightened risk of MACEs within 3 months (natriuretic peptide: OR 3.37, 95% CI 2.07 to 5.47, I^2=87.9%; cardiac troponin: OR 4.89, 95% CI 1.52 to 15.75, I^2=69.5%) with significant heterogeneity. Only natriuretic peptide was associated with a high-risk long-term MACEs (>3 months) (OR 3.52, 95% CI 1.73 to 7.17, I^2=86.2%). In contrast, cardiac biomarkers were not identified as having prognostic value for all-cause mortality in this patient cohort. Additionally, an increased risk of all-cause mortality was associated with preoperative abnormal levels of albumin (OR 1.15, 95% CI 1.06 to 1.24, I^2=84.8%), creatinine (OR 1.54, 95% CI 1.12 to 1.95, I^2=0), 25(OH)D (OR 1.58, 95% CI 1.01 to 2.14, I^2=0) and glomerular filtration rate (GFR) (OR 1.12, 95% CI 1.06 to 1.17, I^2=0), rather than cardiac biomarkers.

Conclusions The study proposed that cardiac biomarkers assessed before surgery could offer prognostic insight into short-term MACEs, while preoperative abnormal levels of albumin, creatinine, 25 (OH)D and GFR might be prognostic valuable for all-cause mortality following major orthopaedic surgery.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The use of a comprehensive search strategy and screening of a large number of studies.
⇒ This systematic review encompasses a comprehensive evaluation of all potential blood-based biomarkers specifically related to major orthopaedic surgery.
⇒ Heterogeneity among the included studies and the potential risk of bias in the reviewed articles may limit the interpretability and applicability of the findings.

PROSPERO registration number CRD42022352091.

INTRODUCTION

Cardiovascular complications frequently arise following major orthopaedic surgery and significant mortality rates can result from major adverse cardiac events (MACEs). Previous studies have shown that major orthopaedic procedures have a perioperative MACE incidence ranging from 5% to 20%.[1–4] Therefore, it is essential to understand the prognosis for these patients. This highlights the need to identify individuals who qualify for interventions to reduce their risk of MACEs and death.

The following classification systems are commonly used to assess and anticipate the risk of perioperative morbidity and mortality, especially those stemming from cardiac issues: the American Society of Anesthesiologists Physical Status (ASA-PS),[5] the revised cardiac risk index (RCRI)[6] and the National Surgical Quality Improvement Program Myocardial Infarction and Cardiac Arrest (NSQIP-MICA).[7] Unfortunately, the literature shows that these scores generally work only moderately well and do not accurately predict mortality risk.[8] Although motor ability serves as a frequent criterion, it can be constrained

by pain or pre-existing conditions.[9] This raises questions about the effectiveness of conventional approaches such as the New York Heart Association (NYHA) Class,[10] Canadian Cardiovascular Society (CCS) angina scores[11] and the 6-minute walking test.[12] As a result, there is an increasing interest in blood-based biomarkers within this context.

Cardiac biomarkers such as troponin (cTn), B-type natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP) have been explored as potential indicators of postoperative MACEs and mortality following non-cardiac surgery.[13] However, the prognostic significance of cardiac biomarkers remains controversial in patients with major orthopaedic surgery. Current recommendations suggest a cautious consideration of cardiac biomarkers in high-risk patients undergoing major non-cardiac surgery.[14] Furthermore, recent studies have delved into several other blood-based biomarkers in major orthopaedic surgery. However, despite the increasing number of studies investigating the prognostic value of blood-based markers in major orthopaedic surgeries, the findings have shown inconsistencies. Therefore, the uncertain acceptance of blood-based biomarkers as reliable prognostic factors for postoperative MACEs and mortality following major orthopaedic surgery persists. Given the limited and inconclusive state of the literature, we conducted a comprehensive meta-analysis and systematic review to investigate the correlation between preoperative blood biomarkers and postoperative MACEs, as well as all-cause mortality in patients undergoing major orthopaedic surgery.

METHODS

This systematic review protocol, conducting and reporting were accomplished following the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines.[15] This systematic review was registered in the PROSPERO database on 8 August 2022 (CRD42022352091).

Patient and public involvement

Patients and the public were not involved in this systematic review. Hence, ethical approval was not required.

Study selection and eligibility criteria

Two investigators conducted independent screenings of eligible studies, and any disagreements were resolved through discussion. We included observational or experimental studies involving adults (>18 years) undergoing major orthopaedic surgery that examined the association between preoperative blood-based biomarkers and postoperative MACEs and/or mortality following major orthopaedic surgery. Major orthopaedic surgery in this study was defined as spinal surgery, knee or hip or ankle arthroplasty, all types of hip fracture surgery, pelvic fracture surgery, shoulder surgery or amputation. Studies were excluded if they were case reports, cross-sectional studies, editorials or letters to the editor, review articles and summaries of conference abstracts. We also excluded studies that did not mention the outcome of interest and studies providing incomplete or invalid information on biomarkers.

Search strategy

A systematic search of PubMed, EMBASE, the Cochrane Controlled Trials Register and Cochrane Database of Systematic Reviews from inception to 20 October 2024 was performed to identify relevant studies using the following search terms: orthopedic surgery, hip fracture, femur fracture, knee, hip, extremity, non-cardiac surgery, biomarkers, complication, cardiovascular and mortality. The detailed search strategy is available in online supplemental appendix 1. No restrictions were imposed. The reference lists of all eligible publications and reviews were scanned to identify additional relevant studies. The computer retrieval was supplemented by hand search of the references of relevant original articles and reviews.

Two authors independently screened and reviewed all titles and abstracts for eligibility. For abstracts that did not provide sufficient information to determine eligibility, full-length articles were retrieved. In all steps, any disagreement regarding eligibility was resolved via discussion between the reviewers and a third investigator as needed.

Data extraction

Studies were reviewed, and data were extracted independently by two authors using a predesigned standard form with any discrepancy being resolved by reinspection of the original article. The primary outcome of interest was postoperative MACEs. MACEs were defined as acute myocardial infarction (AMI), heart failure (HF) and arrhythmia or defined by the study author. Occurrences within 3 months after surgery are termed short-term postoperative MACEs, whereas those happening beyond 3 months are classified as long-term MACEs. In cases where studies lacked follow-up information, we computed the data as postoperative MACEs. The secondary outcome was all-cause mortality as up to the study follow-up time. The study design, patient demographics, biomarkers assays and preoperative history of cardiovascular disease were also extracted. In cases where full-text access is unavailable or there are uncertainties regarding data within an article, we attempt to contact the corresponding author for clarification.

Quality assessment

Two researchers assessed the bias of included articles independently, and any disagreement was solved through discussion. The methodological quality of each study was evaluated using the Quality in Prognostic Studies (QUIPS) tool.[16] The QUIPS tool consists of six domains: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, statistical analysis and reporting. The overall risk of bias was

high if any risk of a single domain was considered as high. Every domain was considered in low risk; the overall risk of bias can be defined as low. The overall risk was moderate in other circumstances.

Statistical analysis

OR and HR for MACEs or all-cause mortality with their associated variances (95% CIs or SEs) were obtained directly from the publication where possible. If studies employed biomarkers with clearly defined cutoff values for analysis, we include the data in the pooled estimate; otherwise, we only present the findings of those studies descriptively in the Results section. When both estimates from univariable and multivariable analyses were available, the estimates obtained by the multivariable analyses were used for further analyses. If no univariable or multivariable effect size was reported by the study, we contacted the authors for detailed information. Pooled estimates with 95% CIs were calculated by the random effects models. The heterogeneity of the studies was assessed with both the Cochran's Q statistics and the I^2 statistic. Publication bias was evaluated using the funnel plot. In the case of significant asymmetry, Duval and Tweedie's trim-and-fill procedure was performed to identify missing studies that should have been plotted. We conducted sensitivity analyses to assess the robustness of the results. Specifically, we assessed whether the results were consistent when (1) only including studies with hip fracture surgery and (2) prospective studies. All statistical analyses were performed in Stata V.16.0. (StataCorp; College Station, Texas, USA).

RESULTS

Study selection

A total of 8847 records were initially identified from the literature search. Figure 1 outlines the screening process. 5291 records were screened after removing the duplicated records. Following title and abstract evaluation, 410 full-text articles underwent eligibility assessment. Out of these, 321 were excluded for various reasons, including non-orthopaedic surgery (n=70), not involving blood-based biomarkers (n=72), not being preoperative biomarkers (n=77), or lacking the relevant outcome (n=102). Through the citation searching, nine further eligible studies were identified. Ultimately, a total of 80 studies published between 2006 and 2024 met all the eligibility criteria.[17–96]

Quality of the enrolled studies

The assessment of individual study quality using the QUIPS tool is summarised in online supplemental figure S1. Out of the 80 studies included, 30 were found to have a high overall risk,[17–19 23 29 31 33 37 46 47 50 56–58 62 67 68 71 73 74 76 78–80 83 85 86 91 95 96] and 35 had a moderate risk.[20–22 26–28 34 38 39 41–43 45 48 51 53–55 59–61 63 64 66 69 72 75 81 87–90 92–94] The distribution of risk across the six domains is presented in figure 2. The bias of confounding was identified as a major concern in

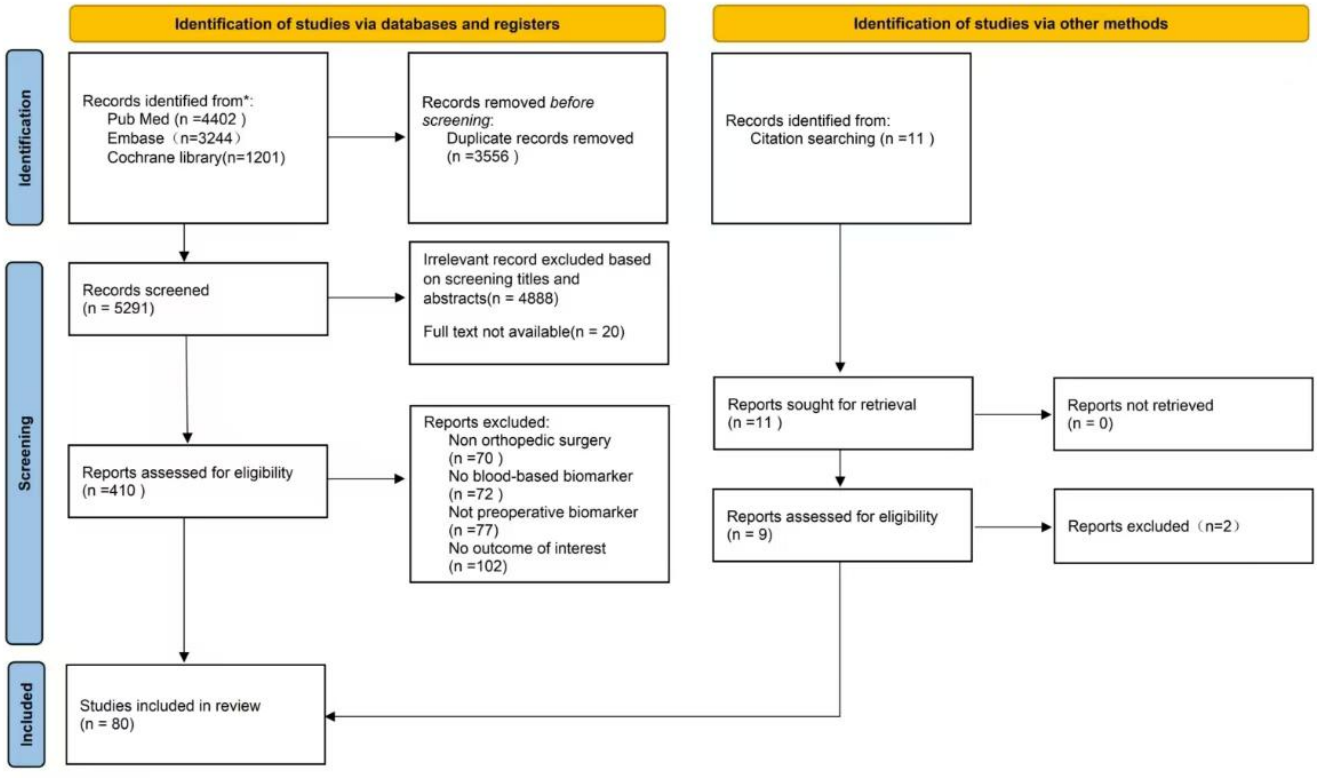

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

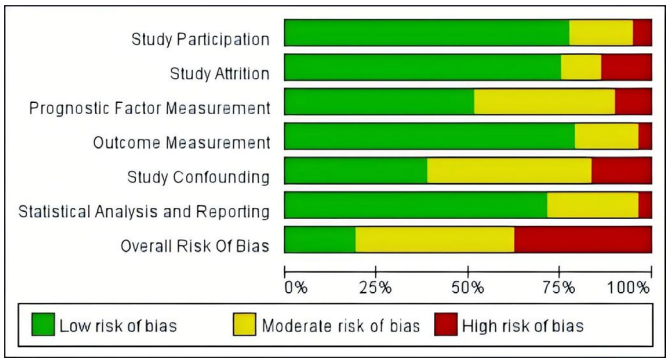

Figure 2 Risk of bias graph: review authors' judgement about each risk of bias item presented as percentages across all included studies.

the majority of the studies, primarily due to the failure to account for important confounders in their study design or the lack of mention regarding the adequacy and reliability of measuring all important confounders. However, in the remaining five domains, most of the included studies demonstrated a low risk of bias.

Study characteristics

The total number of patients was 226 468, with a mean age of 81 years. Online supplemental table S1 provides an overview of the characteristics of these included studies. The studies specifically targeted patients who underwent major orthopaedic surgery, 60 of 80 studies focusing on hip fracture surgery[20–25 27 31–36 39–43 45 47–49 51 53 55–64 66–70 74–79 81–86 88–96] and 7 of 80 studies focusing on hip or knee arthroplasty procedures.[18 52 54 65 72 73 87] The remaining 13 studies focused on spinal surgery or amputation or shoulder arthroplasty or mixed procedures.[17–19 26 28 29 31 37 44 46 50 71 80] 40 of the 80 studies employed a prospective design.[17–22 26 29 31–35 37 39 40 42–45 48–52 56 58 59 62–64 66–70 72 81 84 85] However, the rest 40 studies were retrospective studies.[23–25 27 28 30 36 38 41 46–48 53–55 57 60 61 71 73–80 82 83 86–96] The follow-up periods spanned from 5 days to 9 years. Notably, only 6 of the studies explicitly mentioned the exclusion of patients with pre-existing heart disease.[22 30 36 37 44 51]

Biomarkers assay information

Detailed information about the measurement of biomarkers and adverse outcomes is provided in online supplemental table S2. 48 studies reported the long-term outcomes, and the median follow-up time was 1 year in the range of 3 months to 9 years.[21 23 26–29 32–34 39 40 42–45 47 48 50 52 53 55–57 59 61–63 66 67 70 75–79 81 82 86 87 89–96]

Among the 80 included studies, 13 of them measured NT-proBNP,[21 22 28 29 50 51 59 60 62 66 69 92 96] 7 measured BNP,[26 31 44 52 71 72 74] 13 measured cardiac troponin (Tn T, Tn I and hs-TnI)[22 28 29 33 35 37 45 49–51 67 70 92] and 54 studies measured various other biomarkers[17–20 23–25 27 30 32 34 36 38–43 46–48 53–58 61 63–65 68 73 75–91 93–96] including albumin, creatinine, C-reactive protein (CRP), glomerular filtration rate (GFR), haemoglobin, blood cell counts, platelet CD40L, P-selectin, platelet factor V/Va, 25-Hydroxy-vitamin-D (25(OH)D), bone turnover markers (PINP&β-CTX), cytokines (FLT3LG, CXCL-12, CXCL-8 and IL-7), miR-409–3p and lactate. It is important to note that some of the included studies measured multiple biomarkers.

Primary outcome: MACEs

Cardiac biomarkers

Twelve studies provided adjusted ORs for the association between preoperative BNP or NT-proBNP and MACEs.[22 26 28 29 31 50 62 65 66 69 71 72 92] Using a random-effects model, preoperative elevated levels of BNP or NT-proBNP were associated with higher incidence of short-term MACEs (OR 3.37, 95% CI 2.07 to 5.47, figure 3) and long-term MACEs (OR 2.78, 95% CI 1.21 to 6.40, figure 3). A high degree of heterogeneity was noted across studies (p<0.001 for the Q statistics, I^2=87.9% for short-term and p<0.001 for the Q statistics, I^2=86.2% for long-term). The combined HR from two studies was 1.02 (95% CI 1.005 to 1.035, I^2=0%), indicating a correlation between elevated preoperative levels of BNP or NT-proBNP and an increased occurrence of short-term postoperative MACEs.[44 51] Additionally, one study reported that NT-proBNP is an independent risk factor for long-term MACEs (HR 2.395, 95% CI 1.084 to 5.293).[92]

Data from four studies were provided regarding the association between preoperative cardiac troponin and short-term MACEs.[22 28 50 66] Pooled estimate from those studies demonstrated that elevated preoperative troponin was associated with a significantly higher incidence of short-term MACEs (OR 4.89, 95% CI 1.52 to 15.75, figure 4) which exhibited high heterogeneity (I^2=69.5%, p=0.02 for Q statistics). Regarding long-term MACEs, only two studies provided adjusted ORs. The pooled analysis showed no significant association between preoperative troponin levels and long-term (OR 3.65, 95% CI 0.86 to 15.45, I^2=83.6%, figure 4).[28 92] However, one study which reported adjusted HR showed that preoperative troponin was a significant and adjusted predictor of long-term MACEs (HR 3.48, 95% CI 1.87 to 6.47).[51]

Other biomarkers

In three studies assessing the link between preoperative creatinine and postoperative MACEs,[22 28 62] no significant association was observed (OR 1.00, 95% CI 0.99 to 1.01, I^2=49.8%, online supplemental figure S2). Similarly, three studies investigating the relationship between preoperative GFR and postoperative MACEs found no significant association (OR 0.97, 95% CI 0.95 to 1.00, I^2=0, online supplemental figure S2).[18 19 28] Pooled data from four studies did not reveal a significant association between a preoperative low level of haemoglobin and a higher incidence of MACEs after major orthopaedic surgery (OR 1.38, 95% CI 0.61 to 2.16, I^2=89.9%, online supplemental figure S2).[28 38 46 73] Additionally, two studies exploring the connection between preoperative CRP and postoperative MACEs showed no significant association (OR 1.00, 95% CI 1.00 to 1.01, I^2=0, online supplemental figure S2).[19 65] Ray's study analysed preoperative platelet CD40L, P-selectin and platelet factor V/Va for predicting postoperative MACEs.[65] Platelet CD40L showed a significant association with MACEs (OR 1.58, 95% CI 1.11 to 2.24),

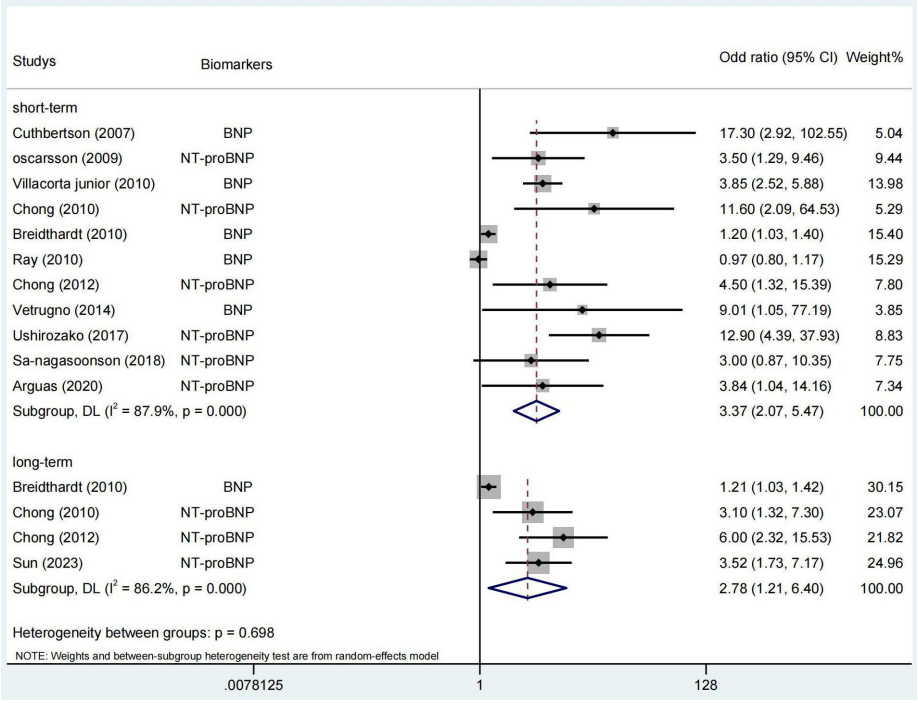

Figure 3 Risk of major adverse cardiac event for patients with elevated preoperative BNP or NT-proBNP versus those with normal levels. BNP, B-type natriuretic peptide; NT-proBNP, N-terminal pro-BNP.

while P-selectin and platelet factor V/Va did not show significant associations. Notably, Sun's study reported that the uncommon biomarker miR-409–3p is an independent risk factor for postoperative long-term MACEs (HR 2.454, 95% CI 1.269 to 4.744).

Secondary outcome: all-cause mortality

Cardiac biomarkers

A total of nine studies investigated the correlation between preoperative BNP and all-cause mortality.[29 31 59 60 62 74 90] One study that did not provide suitable data for meta-analysis found that preoperative higher level of BNP was associated with increased mortality one and 2 years following surgery.[92] Among the remaining studies, six provided adjusted ORs,[29 31 50 60 74 96] while two reported HRs.[59 62] The results from the meta-analysis indicate that elevated preoperative BNP or NT-proBNP is not significantly linked to a higher incidence of all-cause mortality in either the ORs subgroup (OR 1.08, 95% CI 0.89 to 1.32, I^2=78.8%, online supplemental figure S3) or the HRs subgroup (HR 1.44, 95% CI 0.65 to 3.18, I^2=87.9%, online supplemental figure S3).

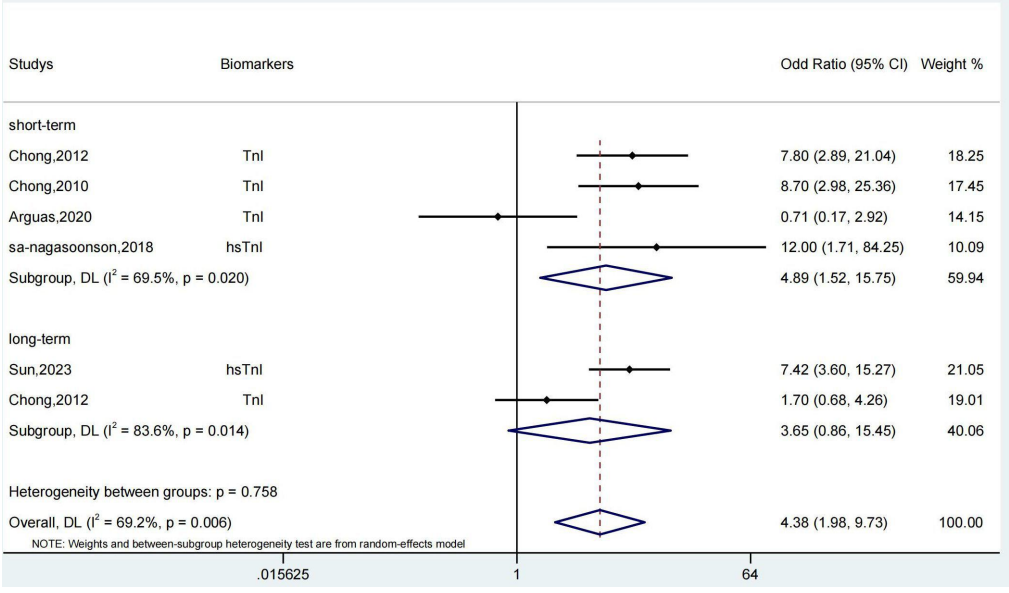

Figure 4 Risk of major adverse cardiac event for patients with elevated preoperative cardiac troponin versus those with normal levels during short-term follow-up.

Eight studies examined the association between preoperative cardiac troponin levels and postoperative all-cause mortality.[29 30 33 35 45 49 67 70] Meta-analysis showed that preoperative troponin elevation was not significantly associated with an increase in postoperative mortality when compared with the reference group (OR 1.20; 95% CI 0.70 to 1.69, online supplemental figure S4), which exhibited moderate heterogeneity (I^2=29.8%, p=0.19 for Q statistics).

Other biomarkers

28 studies investigated the connection between preoperative albumin levels and all-cause mortality after major orthopaedic surgery.[20 23 25 27 30 36 41–43 47 48 53 56–58 61 63 64 68 75 78 80 84 85 87–89 91] Of these, 22 studies provided sufficient data for inclusion in the meta-analysis, and the results indicated a significant association between a lower preoperative albumin level and an increased risk of postoperative mortality compared with the reference group (OR 1.15; 95% CI 1.06 to 1.24, I^2=84.8%, online supplemental figure S5). Among the remaining six studies, five demonstrated a significant association between preoperative hypoalbuminaemia and postoperative mortality,[75 78 84 88 89] while the other one reported a negative result.[91] Pooled data also indicated that higher preoperative serum creatinine levels (OR 1.54; 95% CI 1.12 to 1.95, I^2=0; from four studies, online supplemental figure S5), lower GFR (OR 1.12, 95% CI 1.06 to 1.17, I^2=0; from two studies, online supplemental figure S5) and lower 25(OH)D (OR 1.58, 95% CI 1.01 to 2.14, I^2=0; from three studies, online supplemental figure S5) were significantly associated with an increased risk of postoperative mortality. However, there was no significant association found for preoperative CRP (OR 0.99, 95% CI 0.95 to 1.03, I^2=53.2%; from four studies, online supplemental figure S5) and haemoglobin (OR 1.64, 95% CI 0.51 to 2.77, I^2=82.3%; from five studies, online supplemental figure S5) in relation to postoperative mortality. Additionally, some studies could not be included in the meta-analysis due to insufficient effect size data or an inadequate number of studies. The results of these studies varied. Specifically, three studies on GFR,[83 84 94] two studies each on CRP[78 82] and haemoglobin[83 94] as well as one study on 25(OH)D[76] indicated a significant association between high CRP, low GFR, low 25(OH)D and low haemoglobin levels and postoperative mortality. However, two studies on haemoglobin and creatinine[79 91] and one study on 25(OH)D levels[77] reported negative results regarding their associations with postoperative mortality. Six studies reported on the relationship between blood cell counts and postoperative mortality.[78 79 82 83 91 94] Among three studies on white blood cell count, one showed a significant association with mortality,[83] while two reported a negative result.[79 82] Neither of the two studies on neutrophils found an association with mortality.[78 91] Two studies reported on the association between lymphocyte count and mortality, with one showing a significant association with in-hospital mortality[85] and the other reporting no association.[78] Similarly, two studies examined platelet count and mortality, with one reporting a significant association with mortality[94] and the other finding no association.[91] Notably, three studies reported on less commonly studied biomarkers. Cedeno-Veloz's study examined cytokines (FLT3LG, CXCL-12, CXCL-8 and IL-7) but found no association with postoperative mortality.[81] Olcay's study identified elevated lactate levels as an independent risk factor for 30-day postoperative mortality (HR 1.829, 95% CI 1.229 to 2.577).[88] Wu's study indicated that bone turnover markers (PINP and β-CTX) are independent predictors of postoperative mortality (OR 5.87, 95% CI 1.70 to 23.80 and OR 7.28, 95% CI 2.08 to 29.79).[95]

Sensitivity analysis

We conducted a sensitivity analysis by including only prospective design studies. The significance of the associations between BNP/NT-proBNP and short-term MACE, as well as albumin, BNP/NT-proBNP and troponin with mortality, remained unchanged. However, the association between troponin and short-term MACE as well as BNP/NT-proBNP with long-term MACE became non-significant. Additionally, a sensitivity analysis restricted to patients undergoing hip fracture surgery showed that the associations for BNP/NT-proBNP with short-term MACEs and for albumin, BNP/NT-proBNP and troponin with mortality remained stable, while troponin's association with short-term MACEs became non-significant (see online supplemental figure S2)

Publication bias

Publication bias was evaluated for both MACEs and mortality using funnel plots, as depicted in online supplemental figures S2–S6. Due to potential omissions of studies, the funnel plots for certain outcomes exhibit noticeable asymmetry, strongly suggesting the presence of publication bias. Applying the random-effects model to the filled meta-analysis with the observed studies and the imputed missing studies, the ultimate bias-adjusted estimates of the overall effect size for each outcome remained consistent (see online supplemental table S3).

DISCUSSION

Our systematic review and meta-analysis, encompassing 80 studies, identified 21 preoperative blood-based biomarkers. We found that preoperative cardiac biomarkers were associated with MACEs within 3 months following major orthopaedic surgery but not with long-term MACEs or mortality. Only preoperative natriuretic peptides showed a potential association with MACEs beyond 3 months, though this was not significant in prospective studies and did not extend to mortality. In contrast, elevated risks for all-cause mortality were linked to abnormal preoperative levels of albumin, 25 (OH)D, creatinine and GFR rather than to cardiac biomarkers.

Between 20% and 50% of patients undergoing major non-cardiac surgery exhibit elevated preoperative cardiac

troponin levels.[97 98] A 2019 meta-analysis linked elevated preoperative troponin concentrations to short-term mortality and/or MACE.[99] Additionally, a subsequent prospective cohort study bolstered this association, specifically regarding 30-day and 1-year mortality.[100] The 2022 European Society of Cardiology and 2024 American Heart Association guidelines recommend preoperative troponin measurement for patients with known cardiovascular disease (CVD), those with cardiovascular risk factors (such as age ≥65 years) or those exhibiting symptoms suggestive of CVD who are undergoing elevated risk non-cardiac surgery.[14 101] In contrast, the 2016 Canadian guidelines and the 2023 European Society of Anesthesiology and Intensive Care guidelines do not address preoperative troponin measurement for risk stratification.[102 103] The Canadian guidelines emphasise BNP and NT-proBNP in perioperative evaluation, as these biomarkers are noted for their high negative predictive value.[102] However, a recent cohort study of 3597 patients undergoing non-cardiac surgery found that adding NT-proBNP to traditional risk scores did not significantly improve risk prediction beyond that achieved with risk scores and self-reported functional status alone.[104] Notably, while preoperative cardiac biomarkers show an association with short-term MACEs, their prognostic value diminishes when evaluating long-term MACEs and all-cause mortality in major orthopaedic patients. This disparity may be attributed to various factors. Long-term MACEs are influenced not only by preoperative functional status but also by perioperative factors, including postoperative inflammatory factors and changes in cardiac and kidney function. Similarly, the factors contributing to all-cause postoperative mortality are numerous. Although preoperative cardiac biomarkers are considered predictive for overall mortality in non-cardiac surgical patients, recent guidelines emphasise the low level of evidence. In addition, there is currently no evidence to recommend specific management strategies for patients with elevated preoperative biomarkers to improve perioperative cardiovascular outcomes. Given the unique profiles of orthopaedic patients, especially those undergoing hip fracture repair, spinal surgery or joint replacement, further research is needed to better assess preoperative status objectively. This highlights the importance of considering the evolving cardiovascular risk profile over time after surgery.

Research in the expanding field of the relationship between preoperative biomarkers, extending beyond cardiac biomarkers and postoperative MACEs yields valuable insights into the multifaceted nature of perioperative risk assessment. In the pathophysiology of cardiovascular diseases, inflammatory biomarkers, renal function biomarkers, coagulation biomarkers, haematological biomarkers and metabolic biomarkers, all play crucial roles. Despite this, we did not identify any association between preoperative biomarkers and the incidence of postoperative MACEs. However, our findings reveal that preoperative abnormal levels of albumin, creatinine, 25(OH)D and GFR were associated with all-cause mortality after surgery. This suggests that preoperative biomarkers reflect patients' poor nutritional status, and renal function holds significant prognostic value for all-cause mortality after major orthopaedic surgery.

Notably, the average age of patients included in this study was 81 years. Older age is associated with heightened cardiovascular risk. In the Perioperative Ischaemic Evaluation-2 trial, individuals aged 75 years or older demonstrated a significantly greater risk of postoperative myocardial infarction compared with their younger counterparts (9.5% vs 4.8%; adjusted HR, 1.89 (95% CI, 1.60 to 2.23)).[105] Additionally, non-cardiovascular surgical complications, such as infection, respiratory failure and acute kidney injury, are more prevalent in older adults.[106] However, optimal perioperative care for older adults remains less understood compared with younger individuals. This is partly due to their underrepresentation in clinical trials, with guidelines offering limited cardiovascular care recommendations for this demographic.[107 108] The study did not find cardiac biomarkers to be reliable predictors of all-cause mortality in elderly patients following major orthopaedic surgery. Instead, it suggested that measuring preoperative albumin, creatinine, 25(OH)D and GFR may hold prognostic value for mortality in this population.

Limitation

This review has several limitations that warrant consideration. First, the observed heterogeneity arises from variations in study design, patient populations, definitions of MACEs and biomarker methodologies. Although we conducted sensitivity analyses focusing on prospective studies and those specifically examining hip fractures to address potential heterogeneity, discrepancies in MACE definitions across studies remain a challenge for standardisation. Additionally, differences in biomarker assay types, manufacturers, criteria for biomarker elevation and cutoff thresholds for ORs further contribute to the overall heterogeneity in our analysis. While the sensitivity analyses largely demonstrated the robustness of our findings, variability was noted in the associations between troponins and short-term MACE, as well as between BNP/NT-proBNP and long-term MACE. This variability may stem from the limited number of prospective studies available or the potential lack of significance when controlling for confounding factors. These limitations highlight the need for further research with standardised definitions and methodologies to better assess the prognostic value of cardiac biomarkers in perioperative settings. Second, significant publication bias is evident, largely due to the tendency to selectively report positive findings. Applying the random-effects model to the filled meta-analysis with the observed studies and the imputed missing studies, the ultimate bias-adjusted estimates of the overall effect size for each outcome remained consistent. Finally, our analysis centres on individual preoperative biomarkers, without considering potential shifts in biomarker levels between preoperative and postoperative stages, or the combined predictive value of multiple biomarkers for postoperative adverse events.

In conclusion, our systematic review suggests that preoperative cardiac biomarkers may have prognostic value for MACEs but not for all-cause mortality following major orthopaedic surgical patients and preoperative levels of albumin, creatinine, 25 (OH)D and GFR, rather than cardiac biomarkers may have prognostic value on all-cause mortality. Future research should focus on routine perioperative biomarker testing, preoperative rehabilitation and intraoperative and postoperative management strategies for test-positive patients.

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Contributors YS and YR conceived the idea for the protocol and made the main contribution to planning and preparation of timelines for its completion. YS and ZW planned the data extraction and statistical analysis, as well as of risk of bias, quality of evidence and completeness of reporting assessments. YR designed the tables and wrote the first draft of the manuscript, which was then reviewed and amended by YR, ZW, SZ, LL, ZH and YS. All authors then approved the final written manuscript. YS is the guarantor for the work.

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Competing interests None declared.

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REFERENCES

1 Beckerly R, Avram MJ. Clinical Anesthesia Procedures of the Massachusetts General Hospital, Eighth Edition. *Anesthesiology* 2011;115:663.
2 Swann MC, Hoes KS, Aoun SG, *et al*. Postoperative complications of spine surgery. *Best Pract Res Clin Anaesthesiol* 2016;30:103–20.
3 Borges FK, Bhandari M, Guerra-Farfan E, *et al*. Accelerated surgery versus standard care in hip fracture (HIP ATTACK): an international, randomised, controlled trial. *The Lancet* 2020;395:698–708.
4 Le Manach Y, Collins G, Bhandari M, *et al*. Outcomes After Hip Fracture Surgery Compared With Elective Total Hip Replacement. *JAMA* 2015;314:1159–66.
5 Horvath B, Kloesel B, Todd MM, *et al*. The Evolution, Current Value, and Future of the American Society of Anesthesiologists Physical Status Classification System. *Anesthesiology* 2021;135:904–19.
6 Lee TH, Marcantonio ER, Mangione CM, *et al*. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation* 1999;100:1043–9.
7 Fleisher LA, Fleischmann KE, Auerbach AD, *et al*. 2014 ACC/AHA Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Noncardiac Surgery: Executive Summary. *Circulation* 2014;130:2215–45.
8 Carabini LM, Zeeni C, Moreland NC, *et al*. Predicting major adverse cardiac events in spine fusion patients: is the revised cardiac risk index sufficient? *Spine (Phila Pa 1976)* 2014;39:1441–8.
9 Hodges PW, Tucker K. Moving differently in pain: a new theory to explain the adaptation to pain. *Pain* 2011;152:S90–8.
10 White P, Myers M. THE CLASSIFICATION OF CARDIAC DIAGNOSIS. *JAMA* 1921;77:1414.
11 Campeau L. Letter: Grading of angina pectoris. *Circulation* 1976;54:522–3.
12 Butland RJ, Pang J, Gross ER, *et al*. Two-, six-, and 12-minute walking tests in respiratory disease. *Br Med J (Clin Res Ed)* 1982;284:1607–8.
13 De Hert SG, Lurati Buse GA. Cardiac Biomarkers for the Prediction and Detection of Adverse Cardiac Events After Noncardiac Surgery: A Narrative Review. *Anesth Analg* 2020;131:187–95.
14 Halvorsen S, Mehilli J, Cassese S, *et al*. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. *Eur Heart J* 2022;43:3826–924.
15 Stroup DF, Berlin JA, Morton SC, *et al*. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.
16 Hayden JA, van der Windt DA, Cartwright JL, *et al*. Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013;158:280–6.
17 Ackland GL, Scollay JM, Parks RW, *et al*. Pre-operative high sensitivity C-reactive protein and postoperative outcome in patients undergoing elective orthopaedic surgery. *Anaesthesia* 2007;62:888–94.
18 Ackland GL, Moran N, Cone S, *et al*. Chronic Kidney Disease and Postoperative Morbidity After Elective Orthopedic Surgery. *Anesth Analg* 2011;112:1375–81.
19 Adar A, Onalan O, Cakan F, *et al*. A strong and reliable indicator for early postoperative major cardiac events after elective orthopedic surgery: Aortic arch calcification. *Heart Lung* 2019;48:446–51.
20 Aldebeyan S, Nooh A, Aoude A, *et al*. Hypoalbuminaemia-a marker of malnutrition and predictor of postoperative complications and mortality after hip fractures. *Injury* 2017;48:436–40.
21 Anghelescu D, Popescu E, Mihalcea D, *et al*. The influence of preoperative cardiovascular assessment and time to surgery on postoperative mortality after surgery for femoral neck fractures in elderly patients. *Arch Balk Med Union* 2018;53:551–6.
22 Araguas MA, Herrera A, Garrido I, *et al*. Risk factors for major adverse cardiovascular events after osteoporotic hip fracture repair surgery. *Injury* 2020;51 Suppl 1:S30–6.
23 Atay T, Gokce Ceylan B, Ozmeric A, *et al*. The Effects Of Related Factors On One And Two-year Mortality After A Hip Fracture In Elderly Turkish Patients. *Med J Trakya Univ* 2010;27:127–31.
24 Balta O, Altınayak H, Gürler Balta M, *et al*. Can C-reactive protein-based biomarkers be used as predictive of 30-day mortality in elderly hip fractures?A retrospective study. *Ulus Travma Acil Cerrahi Derg* 2022;28:849–56.
25 Bohl DD, Shen MR, Hannon CP, *et al*. Serum Albumin Predicts Survival and Postoperative Course Following Surgery for Geriatric Hip Fracture. *J Bone Joint Surg Am* 2017;99:2110–8.
26 Breidthardt T, Kindler CH, Schindler C, *et al*. B-type natriuretic peptide in patients undergoing orthopaedic surgery: a prospective cohort study. *Eur J Anaesthesiol* 2010;27:690–5.
27 Cher EWL, Allen JC, Moo IH, *et al*. Sub-optimal serum 25-hydroxyvitamin D level affects 2-year survival after hip fracture surgery. *J Bone Miner Metab* 2020;38:555–62.
28 Chong CP, Lim WK, Velkoska E, *et al*. N-terminal pro-brain natriuretic peptide and angiotensin-converting enzyme-2 levels and their association with postoperative cardiac complications after emergency orthopedic surgery. *Am J Cardiol* 2012;109:1365–73.
29 Chong CP, van Gaal WJ, Ryan JE, *et al*. Troponin I and NT-proBNP (N-terminal pro-brain natriuretic peptide) do not predict 6-month

mortality in frail older patients undergoing orthopedic surgery. *J Am Med Dir Assoc* 2010;11:415–20.
30 Çiçek V, Cinar T, Hayiroglu MI, *et al*. Preoperative cardiac risk factors associated with in-hospital mortality in elderly patients without heart failure undergoing hip fracture surgery: a single-centre study. *Postgrad Med J* 2021;97:701–5.
31 Cuthbertson BH, Card G, Croal BL, *et al*. The utility of B-type natriuretic peptide in predicting postoperative cardiac events and mortality in patients undergoing major emergency non-cardiac surgery. *Anaesthesia* 2007;62:875–81.
32 Dauny V, Thietart S, Cohen-Bittan J, *et al*. Association between Vitamin D Deficiency and Prognosis after Hip Fracture Surgery in Older Patients in a Dedicated Orthogeriatric Care Pathway. *J Nutr Health Aging* 2022;26:324–31.
33 Dawson-Bowling S, Chettiar K, Cottam H, *et al*. Troponin T as a predictive marker of morbidity in patients with fractured neck of femur. *Injury* 2008;39:775–80.
34 Fakler JK, Grafe A, Dinger J, *et al*. Perioperative risk factors in patients with a femoral neck fracture – influence of 25-hydroxyvitamin D and C-reactive protein on postoperative medical complications and 1-year mortality. *BMC Musculoskelet Disord* 2016;17.
35 Fisher AA, Southcott EN, Goh SL, *et al*. Elevated serum cardiac troponin I in older patients with hip fracture: incidence and prognostic significance. *Arch Orthop Trauma Surg* 2008;128:1073–9.
36 Fisher A, Fisher L, Srikusalanukul W, *et al*. Usefulness of simple biomarkers at admission as independent indicators and predictors of in-hospital mortality in older hip fracture patients. *Injury* 2018;49:829–40.
37 Gibson SC, Marsh A, Berry C, *et al*. Should Pre-operative Troponin be a Standard Requirement in Patients Undergoing Major Lower Extremity Amputation? *Eur J Vasc Endovasc Surg* 2006;31:637–41.
38 Grosso MJ, Boddapati V, Cooper HJ, *et al*. The Effect of Preoperative Anemia on Complications After Total Hip Arthroplasty. *J Arthroplasty* 2020;35:S214–8.
39 Gulin T, Kruljac I, Kirigin L, *et al*. Advanced Age, High β-CTX Levels, and Impaired Renal Function are Independent Risk Factors for All-Cause One-Year Mortality in Hip Fracture Patients. *Calcif Tissue Int* 2016;98:67–75.
40 H. Jonsson M, Åkesson A, Hommel A, *et al*. Markers of renal function at admission and mortality in hip fracture patients - a single center prospective observational study. *Scand J Clin Lab Invest* 2021;81:201–7.
41 Harrison SJ, Messner J, Leeder DJ, *et al*. Are Albumin Levels a Good Predictor of Mortality in Elderly Patients with Neck of Femur Fractures? *J Nutr Health Aging* 2017;21:699–703.
42 Helminen H, Luukkaala T, Saarnio J, *et al*. Comparison of the Mini-Nutritional Assessment short and long form and serum albumin as prognostic indicators of hip fracture outcomes. *Injury* 2017;48:903–8.
43 Hershkovitz A, Polatov I, Beloosesky Y, *et al*. Factors affecting mortality of frail hip-fractured elderly patients. *Arch Gerontol Geriatr* 2010;51:113–6.
44 Katsanos S, Babalis D, Kafkas N, *et al*. B-type natriuretic peptide vs. cardiac risk scores for prediction of outcome following major orthopedic surgery. *J Cardiovasc Med (Hagerstown)* 2015;16:465–71.
45 Katsanos S, Mavrogenis AF, Kafkas N, *et al*. Cardiac Biomarkers Predict 1-Year Mortality in Elderly Patients Undergoing Hip Fracture Surgery. *Orthopedics* 2017;40:e417–24.
46 Kaye ID, Wagner SC, Butler JS, *et al*. Risk Factors for Adverse Cardiac Events After Lumbar Spine Fusion. *Int J Spine Surg* 2018;12:638–43.
47 Kieffer WKM, Rennie CS, Gandhe AJ. Preoperative albumin as a predictor of one-year mortality in patients with fractured neck of femur. *Ann R Coll Surg Engl* 2013;95:26–8.
48 Kim B-G, Lee Y-K, Park H-P, *et al*. C-reactive protein is an independent predictor for 1-year mortality in elderly patients undergoing hip fracture surgery. *Medicine (Baltimore)* 2016;95:e5152.
49 Hietala P, Strandberg M, Kiviniemi T, *et al*. Usefulness of troponin T to predict short-term and long-term mortality in patients after hip fracture. *Am J Cardiol* 2014;114:193–7.
50 Chong CP, Ryan JE, van Gaal WJ, *et al*. Usefulness of N-terminal pro-brain natriuretic peptide to predict postoperative cardiac complications and long-term mortality after emergency lower limb orthopedic surgery. *Am J Cardiol* 2010;106:865–72.
51 Kim BS, Kim T-H, Oh J-H, *et al*. Association between preoperative high sensitive troponin I levels and cardiovascular events after hip fracture surgery in the elderly. *J Geriatr Cardiol* 2018;15:215–21.
52 Long G, Hao C, Li G, *et al*. Predictive value of B-type natriuretic peptide (BNP) for adverse cardiac events in patients undergoing primary total knee arthroplasty (TKA). *J Orthop Sci* 2016;21:826–30.
53 Lu J. Laboratory nutritional parameters can predict one-year mortality in elderly patients with intertrochanteric fracture. *JNHFS* 2014;2:457–63.
54 Lu M, Sing DC, Kuo AC, *et al*. Preoperative Anemia Independently Predicts 30-Day Complications After Aseptic and Septic Revision Total Joint Arthroplasty. *J Arthroplasty* 2017;32:S197–201.
55 McLeod G, Kennedy I, Simpson E, *et al*. Pilot Project for a Web-Based Dynamic Nomogram to Predict Survival 1 Year After Hip Fracture Surgery: Retrospective Observational Study. *Interact J Med Res* 2022;11:e34096.
56 Miu KYD, Lam PS. Effects of Nutritional Status on 6-Month Outcome of Hip Fractures in Elderly Patients. *Ann Rehabil Med* 2017;41:1005–12.
57 Miyanishi K, Jingushi S, Torisu T. Mortality after Hip Fracture in Japan: The Role of Nutritional Status. *J Orthop Surg (Hong Kong)* 2010;18:265–70.
58 Mosfeldt M, Pedersen OB, Riis T, *et al*. Value of routine blood tests for prediction of mortality risk in hip fracture patients. *Acta Orthop* 2012;83:31–5.
59 Nordling P, Kiviniemi T, Strandberg M, *et al*. Predicting the outcome of hip fracture patients by using N-terminal fragment of pro-B-type natriuretic peptide. *BMJ Open* 2016;6:e009416.
60 Norring-Agerskov D, Madsen CM, Bathum L, *et al*. History of cardiovascular disease and cardiovascular biomarkers are associated with 30-day mortality in patients with hip fracture. *Osteoporos Int* 2019;30:1767–78.
61 O'Daly BJ, Walsh JC, Quinlan JF, *et al*. Serum albumin and total lymphocyte count as predictors of outcome in hip fractures. *Clin Nutr* 2010;29:89–93.
62 Oscarsson A, Fredrikson M, Sörliden M, *et al*. N-terminal fragment of pro-B-type natriuretic peptide is a predictor of cardiac events in high-risk patients undergoing acute hip fracture surgery. *Br J Anaesth* 2009;103:206–12.
63 Oztürk A, Ozkan Y, Akgöz S, *et al*. The effect of blood albumin and total lymphocyte count on short-term results in elderly patients with hip fractures. *Ulus Travma Acil Cerrahi Derg* 2009;15:546–52.
64 Pimlott BJ, Jones CA, Beaupre LA, *et al*. Prognostic impact of pre-operative albumin on short-term mortality and complications in patients with hip fracture. *Arch Gerontol Geriatr* 2011;53:90–4.
65 Ray MJ, Calabro LJ, Sirisena T, *et al*. Pre-operative platelet-bound CD40 ligand is probably associated with peri-operative cardiac events in hip and knee arthroplasty. *Eur J Clin Invest* 2010;40:497–503.
66 Sa-Ngasoongsong P, Thamyongkit S, Kulachote N, *et al*. Usefulness of Serum Cardiac Biomarkers for Predicting In-Hospital Cardiac Complications in Acute Hip Fracture: A Prospective Cohort in 20 High Surgical Risk patients with Age over 55 Years. *Biomed Res Int* 2018;2018:3453652.
67 Spurrier E, Wordsworth D, Martin S, *et al*. Troponin T in hip fracture patients: prognostic significance for mortality at one year. *Hip Int* 2011;21:757–61.
68 Uriz-Otano F, Pla-Vidal J, Tiberio-López G, *et al*. Factors associated to institutionalization and mortality over three years, in elderly people with a hip fracture-An observational study. *Maturitas* 2016;89:9–15.
69 Ushirozako H, Ohishi T, Fujita T, *et al*. Does N-terminal Pro-brain Type Natriuretic Peptide Predict Cardiac Complications After Hip Fracture Surgery? *Clin Orthop Relat Res* 2017;475:1730–6.
70 Vallet H, Breining A, Le Manach Y, *et al*. Isolated cardiac troponin rise does not modify the prognosis in elderly patients with hip fracture. *Medicine (Baltimore)* 2017;96:e6169.
71 Vetrugno L, Langiano N, Gisonni R, *et al*. Prediction of early postoperative major cardiac events after elective orthopedic surgery: the role of B-type natriuretic peptide, the revised cardiac risk index, and ASA class. *BMC Anesthesiol* 2014;14:20.
72 Villacorta JH, Castro IS, Godinho M, *et al*. B-type natriuretic peptide is predictive of postoperative events in orthopedic surgery. *ARQ Bras Cardiol* 2010;95:743–8.
73 Viola J, Gomez MM, Restrepo C, *et al*. Preoperative anemia increases postoperative complications and mortality following total joint arthroplasty. *J Arthroplasty* 2015;30:846–8.
74 Zhao F, Wang X, Dou Y, *et al*. Analysis of risk factors for perioperative mortality in elderly patients with intertrochanteric fracture. *Eur J Orthop Surg Traumatol* 2019;29:59–63.
75 Thomas BK, Bajada S, Williams RL. Albumin is an Independent Predictor of up to 9-Year Mortality for Intracapsular Femoral Neck Fractures Aiding in Decision-Making for Total Hip Arthroplasty or Hemiarthroplasty. *J Arthroplasty* 2023;38:135–40.

76 Fu G, Wu R, Zhang R, *et al*. Preoperative Vitamin D Deficiency is Associated with Increased One-Year Mortality in Chinese Geriatric Hip Fracture Patients - A Propensity Score Matching Study. *Clin Interv Aging* 2023;18:263–72.
77 Hao L, Carson JL, Schlussel Y, *et al*. Vitamin D deficiency is associated with reduced mobility after hip fracture surgery: a prospective study. *Am J Clin Nutr* 2020;112:613–8.
78 Aydın A, Kaçmaz O. CRP/albumin ratio in predicting 1-year mortality in elderly patients undergoing hip fracture surgery. *Eur Rev Med Pharmacol Sci* 2023;27:8438–46.
79 Babagoli M, Ghaseminejad Raeini A, Sheykhvatan M, *et al*. Influencing factors on morbidity and mortality in intertrochanteric fractures. *Sci Rep* 2023;13.
80 Buzney CD, Zhong H, Gulotta LV, *et al*. Is There Synergistic Effect Between Obesity and Hypoalbuminemia on Postoperative Outcomes Among Primary Total Shoulder Arthroplasty Recipients? *HSS J* 2022;18:504–11.
81 Cedeno-Veloz B, Lozano-Vicario L, Rodríguez-García A, *et al*. Serum biomarkers related to frailty predict negative outcomes in older adults with hip fracture. *J Endocrinol Invest* 2024;47:729–38.
82 Chen Y, Tu C, Liu G, *et al*. Association between admission inflammatory indicators and 3-year mortality risk in geriatric patients after hip fracture surgery: a retrospective cohort study. *Front Surg* 2024;11:1440990.
83 Cheng T-A, Lai P-H, Chuang H-C, *et al*. Predictors of in-hospital mortality in older patients undergoing distal femur fracture surgery: A case-control study. *SICOT J* 2023;9:36.
84 de Haan E, Roukema GR, van Rijckevorsel VAJIM, *et al*. Risk Factors for 30-Days Mortality After Proximal Femoral Fracture Surgery, a Cohort Study. *Clin Interv Aging* 2024;19:539–49.
85 Geleit R, Bence M, Samouel P, *et al*. Biomarkers as predictors of inpatient mortality in fractured neck of femur patients. *Arch Gerontol Geriatr* 2023;111:105004.
86 Guerra MTE, Wagner M, Vargas A, *et al*. Low serum levels of vitamin D significantly increase the risk of death in older adults with hip fractures: a prospective cohort. *Rev Col Bras Cir* 2022;49:e20223054.
87 Guntin J, Serino J, Rossi D, *et al*. Hypoalbuminemia Increases Mortality after Two-Stage Revision Total Joint Arthroplasty. *Arch Bone Jt Surg* 2023;11:173–9.
88 Olcay HÖ, Emektar E, Öztürk ZS, *et al*. Association of Serum Lactate Levels Measured in the Emergency Department with 30-Day Mortality in Older Patients with Unilateral Hip Fractures. *Ann Geriatr Med Res* 2024;28:301–6.
89 Özel M, Altıntaş M, Tatlıparmak AC. Predictors of one-year mortality following hip fracture surgery in elderly. *PeerJ* 2023;11:e16008.
90 Page BJ, Hughes JL, Walsh JM, *et al*. Association of Brain Natriuretic Peptide Levels at Time of Injury with Morbidity and Mortality in Patients with Surgically Treated Hip Fractures. *JB JS Open Access* 2023;8:e22.00102.
91 Rutenberg TF, Hershkovitz A, Jabareen R, *et al*. Can nutritional and inflammatory indices predict 90-day mortality in fragility hip fracture patients? *SICOT J* 2023;9:30.
92 Sun Z, Cheng K, Jin G, *et al*. Increasing serum miR-409-3p predicts the major adverse cardiac adverse events in elderly patients after hip fracture surgery. *BMC Musculoskelet Disord* 2023;24.
93 Wang Z, Zhang L, Zeng X, *et al*. The Nomogram Model and Factors for the Postoperative Mortality of Elderly Patients with Femoral Neck Fracture Undergoing Artificial Hip Arthroplasty: A Single-Institution 6-Year Experience. *Orthop Surg* 2024;16:391–400.
94 Wu C-Y, Tsai C-F, Yang H-Y. Utilizing a nomogram to predict the one-year postoperative mortality risk for geriatric patients with a hip fracture. *Sci Rep* 2023;13.
95 Wu R, Ma Y, Chen D, *et al*. Bone turnover biomarkers predict one-year all-cause mortality and walking ability in geriatric hip fracture patients. *Bone* 2023;177:S8756-3282(23)00255-7.
96 Zhang BF, Ren SB, Wang MX. The Predictive Value of Serum NT-proBNP on One-Year All-Cause Mortality in Geriatrics Hip Fracture: A Cohort Study. *Cureus* 2023;15:e45398.
97 Writing Committee for the VISION Study Investigators, Devereaux PJ, Biccard BM, *et al*. Association of Postoperative High-Sensitivity Troponin Levels With Myocardial Injury and 30-Day Mortality Among Patients Undergoing Noncardiac Surgery. *JAMA* 2017;317:1642–51.
98 Shen J-T, Xu M, Wu Y, *et al*. Association of pre-operative troponin levels with major adverse cardiac events and mortality after noncardiac surgery: A systematic review and meta-analysis. *Eur J Anaesthesiol* 2018;35:815–24.
99 Humble CAS, Huang S, Jammer I, *et al*. Prognostic performance of preoperative cardiac troponin and perioperative changes in cardiac troponin for the prediction of major adverse cardiac events and mortality in noncardiac surgery: A systematic review and meta-analysis. *PLoS ONE* 2019;14:e0215094.
100 Puelacher C, Lurati Buse G, Seeberger D, *et al*. Perioperative Myocardial Injury After Noncardiac Surgery: Incidence, Mortality, and Characterization. *Circulation* 2018;137:1221–32.
101 Thompson A, Fleischmann KE, Smilowitz NR, *et al*. 2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM Guideline for Perioperative Cardiovascular Management for Noncardiac Surgery: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2024;150:e351–442.
102 Duceppe E, Parlow J, MacDonald P, *et al*. Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery. *Can J Cardiol* 2017;33:17–32.
103 Lurati Buse G, Bollen Pinto B, Abelha F, *et al*. ESAIC focused guideline for the use of cardiac biomarkers in perioperative risk evaluation. *Eur J Anaesthesiol* 2023;40:888–927.
104 Lurati Buse G, Larmann J, Gillmann H-J, *et al*. NT-proBNP or Self-Reported Functional Capacity in Estimating Risk of Cardiovascular Events After Noncardiac Surgery. *JAMA Netw Open* 2023;6:e2342527.
105 Devereaux PJ, Mrkobrada M, Sessler DI, *et al*. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014;370:1494–503.
106 Hamel MB, Henderson WG, Khuri SF, *et al*. Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery. *J Am Geriatr Soc* 2005;53:424–9.
107 Chow WB, Rosenthal RA, Merkow RP, *et al*. Optimal preoperative assessment of the geriatric surgical patient: a best practices guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. *J Am Coll Surg* 2012;215:453–66.
108 Mohanty S, Rosenthal RA, Russell MM, *et al*. Optimal Perioperative Management of the Geriatric Patient: A Best Practices Guideline from the American College of Surgeons NSQIP and the American Geriatrics Society. *J Am Coll Surg* 2016;222:930–47.