The accuracy of pre-operative (P)-POSSUM scoring and cardiopulmonary exercise testing in predicting morbidity and mortality after pancreatic and liver surgery: A systematic review

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ABSTRACT

Background: Cardiopulmonary exercise-testing (CPET) and the (Portsmouth) Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity ((P)-POSSUM) are used as pre-operative risk stratification and audit tools in general surgery, however, both have been demonstrated to have limitations in major hepatopancreatobilary (HPB) surgery.

Materials and methods: The aim of this review is to determine if CPET and (P)-POSSUM scoring systems accurately predict morbidity and mortality. Eligible articles were identified with an electronic database search. Analysis according to surgery type and tool used was performed.

Results: Twenty-five studies were included in the final review. POSSUM predicted morbidity demonstrated weighted O/E ratios of 0.75(95%CI0.57–0.97) in hepatic surgery and 0.85(95%CI0.8–0.9) in pancreatic surgery. P-POSSUM predicted mortality in pancreatic surgery demonstrated an O/E ratio of 0.75(95%CI0.27–2.13) and 0.94(95%CI0.57–1.55) in hepatic surgery. In both pancreatic and hepatic surgery an anaerobic threshold(AT) of between 9 0.5–11.5 ml/kg/min was predictive of post-operative complications, and in pancreatic surgery ventilatory equivalence of carbon dioxide(\(\dot{V}E/\dot{V}CO_2\)) was predictive of 30-day mortality.

Conclusion: POSSUM demonstrates an overall lack of predictive fit for morbidity, whilst CPET variables provide some predictive power for post-operative outcomes. Development of a new HPB specific risk prediction tool would be beneficial; the combination of parameters from POSSUM and CPET, alongside HPB specific markers could overcome current limitations.

1. Introduction

Hepatopancreaticobiliary (HPB) surgical procedures are often complex providing both a technical challenge to the surgeon and a significant physiological insult to the patient [1]. Despite improvements with both mortality and medical complications, procedure-specific complications remain a significant source of morbidity [1–3].

Appropriate risk-stratification can enable patients to be better informed, improve patient selection and treatment planning; and therefore, overall outcomes. There are, however, limitations to current risk stratification tools.

The application of the POSSUM (Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity) model has been shown to demonstrate a significant lack of fit for predicting both morbidity and mortality after hepatic and pancreatic surgery. Despite adjustments with the logistic regression used in the Portsmouth (P)-POSSUM iteration to better predict mortality previous reviews have recommended further modifications to improve its usefulness [4,5].

Attempts to develop newer risk-stratification have seen some successes with improved prediction of mortality; the surgical outcome risk score (SORT) was modelled on UK national NCEPOD data. A model of 45 risk factors was refined on repeated regression analysis to develop a model comprising six variables. It demonstrated an AUC of 0.91 in predicting 30 day mortality for a general surgical cohort, though there was still some lack of fit when looking only at a HPB cohort (AUC 0.82) [6].
More recently, cardiopulmonary exercise testing (CPET) has been proposed as a tool in planning major intra-abdominal surgery [7,8]. CPET provides a global assessment of the cardiopulmonary system’s ability to deliver oxygen to tissues under stress, objectively determining the functional reserve [9]. It utilises dynamic pre-operative parameters to provide post-operative predictions; this contrasts the approach used by (P)-POSSUM, which provides post-operative predictions based on static parameters at the pre-operative setting. The rational to the use of CPET is that patients with a higher cardiopulmonary reserve will be better able to compensate and achieve sufficient tissue oxygen delivery post-operatively, thus will recover quicker with a lower risk of post-operative complications [9,10]. It is currently used as an adjunct to decision making but its role hasn’t been clarified [11].

An up to date systematic review was conducted to assess the power of both (P)-POSSUM and CPET to predict post-operative outcomes in major hepatobiliary and pancreatic surgery. The aim of the review is to evaluate the value of each tool individually in predicting both morbidity and mortality, then identify variables within CPET that demonstrate significant value in predicting post-operative morbidity. This could potentially be integrated into a new scoring system to enable better risk stratification in HPB surgery.

2. Methods

2.1. Search strategy

This systematic review followed PRISMA guidelines (Fig. 1) and AMSTAR (Assessing the methodological quality of systematic reviews) guidelines. Pubmed, Embase and the Cochrane Library were searched without time limits up to 2019 using pre-determined search words. Boolean Operations (AND, OR) combined “POSSUM”, “P-POSSUM” or “CPET” with each of the following: “Hepatobiliary”, “Hepatic”, “Liver”, “Gallbladder”, “Pancreas”, “pancreatic”, “Risk”, “Morbidity”, “Mortality” and “Surgery”. Bibliographies of the included papers were searched to identify additional studies.

2.2. Criteria for inclusion and exclusion

Papers were included if they were: retrospective or prospective cohort studies examining either POSSUM, P-POSSUM or CPET in HPB surgery; reported morbidity and/or mortality outcomes; available in English. Studies reviewing (P)-POSSUM had to provide sufficient data with quantification of observed and expected events. For studies reviewing CPET, inclusion required there to be adequate enumeration of the CPET variables of interest, whether this was AT or VE/VCO2. All studies had to provide an adequate quantification of outcomes. Studies in abstract form (n = 1) were included if they contained sufficient data. Studies were excluded if they were: case reports, review articles or other non-original research; included non-major or transplant surgery; included inadequate data to make reasonable comparison. When there was suspicion of studies containing duplicate data, the most recent data was included.

2.3. Review procedure

Two reviewers (VDB and JD) independently screened titles and abstracts; full-text articles were then assessed for eligibility. Any disagreements were resolved by a third independent reviewer (VSY).

The following information was extracted from the papers: author, year of publication, cohort size, study setting, operation type, CPET and (P)-POSSUM variables, post-operative outcome measures including morbidity, as defined by all definitions, mortality and length of stay, and the statistics used to assess the accuracy of each model including measures of significance.

2.4. Synthesis of results

Due to the heterogeneity of the included studies, the individual risk assessment tools were analysed separately. The primary outcome measures were 30-day mortality rates, and morbidity, based on all definitions. The secondary outcome measure was length of hospital stay (LOS).

The accuracy of POSSUM in predicting morbidity and mortality was assessed with observed event to expected event (O/E) ratios. The
weighted observed to expected (O/E) ratios with 95% confidence interval (CI) were calculated using random effects modelling. All studies were weighted with regards to sample size, regardless of other variables such as definition of morbidity or mortality. Analysis included both the POSSUM and P-POSSUM models. An O/E ratio < 1 demonstrates model overprediction whilst > 1 implies model underprediction of events. Sub-analysis for pancreatic and liver surgery was performed (Supplementary Fig. 1). Statistical analysis was performed using Review Manager (RevMan) Version 5.3. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

There was marked heterogeneity in the CPET studies included and consequently a pooled analysis was not feasible, instead descriptive analysis according to hepatic or pancreatic surgery was performed.

3. Results

Three-hundred and seventy titles were identified using the search strategy outlined above. After the removal of duplicates (80) and screening of titles and full text-articles (290), twenty-five full text articles were included in this systematic review. (Fig. 1).

Sixteen studies reviewed the use of (P)-POSSUM scores in predicting post-operative morbidity (n = 12 studies), and mortality (n = 11 studies) after major hepatopancreatobiliary surgery (Table 1–3). Four studies reported morbidity based on the original POSSUM definitions [16,19,22,23]. One referred to the International Study Group of Pancreatic Surgery (ISGPS) definitions of complications after pancreatectomy [17]. Four studies identified morbidity according to the Clavien-Dindo (CD) classification [15,16,20,21], and three used an arbitrary list of complications [12–14].

Nine papers reviewed CPET in predicting post-operative morbidity (n = 6) and mortality (n = 5) in HPB surgery; study characteristics are summarized in Table 4. The anaerobic threshold (AT) and ventilatory equivalent of CO₂ (VE/CO₂) were the most commonly reported variables reviewed with respect to outcome measures including, morbidity, by any definition, mortality, and length of hospital stay (LOS). All studies analysed reported data retrospectively (see Table 5).

3.1. POSSUM

The observed morbidity in major pancreatic surgery ranged from 32.4% to 51.4%, while the POSSUM-predicted morbidity ranged from 36.13% to 76%. The weighted O/E ratio for morbidity in POSSUM in pancreatic surgery was 0.85 (95% CI 0.8–0.9). The observed mortality in major pancreatic surgery ranged from 1.2% to 4%, whilst the POSSUM predicted mortality ranged from 8.7% to 23.7%. The weighted O/E ratio was 0.21 (95% CI 0.09–0.51) (Tables 1a and 2a).

The observed morbidity in major hepatic surgery ranged from 34.7% to 52.0%, while the POSSUM-predicted morbidity ranged from 52.0% to 63.5%. The weighted O/E ratio for morbidity for POSSUM in hepatic surgery was 0.75 (95% CI 0.57–0.97). Whereas the observed mortality in major hepatic surgery ranged from 6.6% to 11.2%, and POSSUM predicted mortality ranged from 9% to 23.7%, producing a weighted O/E ratio of 0.56 (95% CI 0.36–0.88) (Tables 1b and 2b).

3.2. P-POSSUM

The observed mortality for major pancreatic surgery ranged from 1.2% to 7.8%, whilst P-POSSUM predicted mortality ranged from 2.29% to 6.5%. The weighted O/E ratio was 0.75 (95% CI 0.27–2.13); though this was skewed by the larger study by Tamijmarane et al. [12] The observed mortality for major hepatic surgery ranged from 3.95% to 10% and P-POSSUM predicted mortality ranged from 4.2% to 12.9%; the weighted O/E ratio was 0.94 (95% CI 0.57–1.55). Three out of the four papers demonstrated equivocal fit (Tables 3a and 3b).

3.3. CPET in pancreatic surgery

3.3.1. Morbidity

Two studies reported AT as a significant predictor of both morbidity and LOS after PD; pancreatic leaks were analysed in both studies as defined by ISGPS [32,33]. In a cohort of 100 patients undergoing PD or total pancreatectomy (TP), Chandrahalan et al. demonstrated patients with an AT < 10 ml/kg/min had higher incidences of pancreatic fistula, 35.4%, compared to 16% in patients with AT > 10 ml·kg⁻¹·min⁻¹ (p = 0.028). The same AT was also associated with prolonged LOS; 20 days vs 14 day (p = 0.005), with a hazard ratio of 1.74; [CI: 1.14–2.65] [33].

Ausania and colleagues found an AT ≤10.1 ml/kg/min to be associated with pancreatic leak [OR of 5.79 (CI 1.62–20.63) (p = 0.007)], with a 45% leak rate compared to 19.2% in patients with an AT > 10.1 ml/kg/min (p = 0.020) [31]. An AT of ≤ or > 10.1 ml/kg/min also showed a significant difference in predicting any post-operative complication, with 70% compared to 38.5% of patients experiencing a complication (p = 0.013). The same AT was also predictive for length of hospital stay; 29.4 days compared to 17.5 days (p = 0.001) [25]. However, they demonstrated no significant difference in peak VE/VCO₂ between patients who had a pancreatic leak from day 3 post-surgery and those that did not 35.9% vs 37%, (p = 0.409) [32].

3.3.2. Mortality

Junejo et al. demonstrated a VE/VCO₂ of ≥41.0 at AT to be an independent predictor of 30-day mortality in patients undergoing PD [OR 1.35; CI: 1.03–1.77, p = 0.030] and in-hospital mortality [OR 1.26; CI 1.06–1.53] (p = 0.013) [11]. Conversely, when assessing the relationship between AT and mortality, Chandrahalan et al. found no association. [HR 0.77; CI 0.16–3.61] (p = 0.74) [33].

Table 1a

Studies of POSSUM for post-operative morbidity in patients undergoing major Pancreatic surgery.

| Study               | Year | Country | Patients | Operation          | POSSUM | O/E ratio | Comments          |
|--------------------|------|---------|----------|--------------------|--------|-----------|-------------------|
| Tamijmarane et al.  | 2008 | UK      | 241      | PD                 | 44.8   | 36.13     | 1.24              |
| Khan et al.         | 2003 | UK      | 50       | PD                 | 46     | 76        | 0.66              |
| Doblina et al.      | 2011 | Poland  | 65       | PD                 | 32.4   | 64.3      | 0.5               |
| Pratt et al.        | 2008 | US      | 326      | Pancreatic resection | 53.1   | 55.5      | 0.96              |
| Zhang et al.        | 2009 | China   | 265      | PD                 | 39.6   | 43.8      | 0.9               |
| Knight et al.       | 2010 | UK      | 99       | Pancreatic resection | 40.9   | 47.6      | 0.86              |
| De Castro et al.    | 2009 | Netherlands | 652 | PD                 | 50.9   | 57.8      | 0.88              |
| Ruckett et al.      | 2014 | Germany | 697      | PD                 | 43.6   | 58.9      | 0.74              |
| Gallacher et al.    | 2011 | UK      | 81       | PD                 | 54.1   | 63.5      | 0.86              |
3.4. CPET in hepatic surgery

Six studies examined AT, but only one was a randomised controlled trial with the primary outcome measure as surgical morbidities [28]; though it was reported differently amongst them, associations were shown between AT and complications [29,30], length of stay [28,30], and mortality [31,35]. Five of the included papers reported data on VE/VCO2; two papers reported associations between VE/VCO2 and morbidity [31,34].

3.4.1. Morbidity

In this single-centre randomised controlled trial, Dunne et al. found...
that AT was not independently associated with post-operative CD grade III-IV complications (OR of 1.02 (CI 0.90–1.16, p = 0.760)) in 197 patients undergoing major hepatic resection; although it was associated with a reduced LOS, [hazard ratio 2.15 (CI 1.18–3.89) (p = 0.013)] [28]. Similarly, Ulyett et al. showed that mean AT was not significant in predicting CD grade following liver resection (12.8 vs 12.5) (p = 0.84) [34].

Contrary to this, Kairobi et al. found patients with an AT 11.5 ml/kg/min had a relative risk of 2.73 of complication free survival compared to patients with an AT <11.5 ml/kg/min (p = 0.0148) [29] and Kasivisvanathan et al. demonstrated an AT 10.2 ml/kg/min predicts POMS defined morbidity in patients requiring a major hepatic resection [30].

Two studies assessing VE/VCO2 found the measure to be effective in predicting post-operative morbidity. Junejo et al. found that VE/VCO2 of 34.5 or more to be an independent predictor of all post-operative complications (OR 3.97, CI 1.44–10.96, P = 0.008) [31], Ulyett et al. also found the measure to be predictive of CD III-IV complications, OR 1.09 (CI 1.01–1.17, p = 0.04) [34].

4. Discussion

There is evidence that the POSSUM and its P-POSSUM derivative demonstrate a lack of fit in stratifying patients for HPB surgery [4,5]. Our findings supported that POSSUM is a poor predictor of both morbidity and mortality in pancreatic and hepatic surgical cohorts, whereas the predictive power of P-POSSUM was variable. In hepatic surgery P-POSSUM suggested a good predictive power for assessing mortality risk in hepatic surgery. However, it was less accurate in predicting mortality in pancreatic surgery cohorts. Given this lack of fit they lose their reliability in guiding surgical decision making.

There are a number of reasons why the POSSUM models are inadequate in risk-stratification for HPB surgery. Initially constructed for general surgical populations, they fail to adequately account for the complexity of HPB surgery. The weakness introduced through weighting the degree of surgical complexity is evident in the paper by Tamijmarane et al. the assignment of PD as major rather than major complex led to a gross underestimation of morbidity as evidenced by the lowest predicted operative score amongst the papers included (13.67 ± 3.42) [12]. Their observed morbidity was well within the accepted range, yet this was the only study to underestimate post-operative morbidity. Furthermore, others have suggested that additional risk factors such as serum bilirubin, and INR are important prognostic factors and should be included in any modification, [18,23]. Yet these are not implemented.

The rationale for reviewing CPET alongside (P)-POSSUM is that, whereas POSSUM includes only static indices, CPET is a dynamic model of a patient’s ability to adequately compensate for the physiological stress they may encounter when undergoing major surgery. HPB surgery exposes patients to a significant physiological stress; in addition to the complexity of surgery. The added value provided by CPET, may enable identification of patients who will not tolerate the oxygen supply deficit they are exposed to post-operatively.

This review identified two CPET parameters, the AT and VE/VCO2, that may provide significant predictive power for post-operative outcomes. In pancreas surgery, three papers looked at post-operative morbidity according to ISGPS defined complications, meaning other non-pancreas surgery specific complications were not accounted for, limiting the meaningfulness of the results. However, an AT of less than 10–10.1 ml kg−1 min−1 was found to be predictive of grade A-C pancreatic leaks and to be associated with increased hospital length of stay [32,33]. Conversely, Junejo et al. found no association of AT with morbidity [11]. There was significant heterogeneity in the studies reviewing CPET in hepatic surgery, despite this an AT of less than 9.9–11.5 ml kg−1 min−1 appears likely to be predictive of post-operative morbidity as well increased length of stay. Its predictive value for mortality is less clear. Whilst a higher VE/VCO2 was demonstrated by two studies to be predictive of morbidity in major hepatic surgery, its value was not supported by others in predicting either morbidity or mortality [28,30,35].

Previous systematic reviews have also reported AT to be a useful parameter for predicting outcomes in non-HPB cohorts, identifying an AT cut-off similar to that reported in this review [36]. The overall conclusion is that VE/VCO2 is a less reliable predictor of post-operative outcomes.

The heterogeneity of the studies included is a major limitation. For CPET, statistical analysis was inappropriate due to the variability in studies; therefore, only a qualitative approach could be applied. The usefulness of individually reported results is not affected, however, the heterogeneity of the morbidity classification and CPET variables assessed across the available studies severely restricted the ability to draw clear conclusions. To yield future meaningful comparison among studies investigating morbidities and mortalities after HPB procedures, there is a need to standardize complication reporting [37,38]. Another limitation that is difficult to quantify is that of patient selection. CPET is typically done in the pre-operative assessment of patients subjectively deemed to be high risk, therefore a population of low-risk patients were not included in the CPET studies. It was unclear in the selected studies what threshold was used for these HPB patients, as such this introduces a potential source of bias.

Previous literature has concluded the need for an HPB specific revision of the current risk stratification tools. In other specialties attempts have been made to integrate the use of CPET variables within existing tools; the Rassi score is a model that accurately predicts the risk of mortality in Chagas cardiomyopathy, integration of AT increased the accuracy of mortality prediction by 5% [39]. Similarly in major abdominal vascular surgery Thompson et al. demonstrated a significant predictive value of CPET alongside the APACHE II and Detsky scores in predicting both 30-day outcomes and long term survival [40].

This review confirms the limitations of the tools currently being used

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**Table 4**

| Study          | Year | Country | Patients | Operation       | Format       | CPET method | Comments         |
|---------------|------|---------|----------|-----------------|--------------|-------------|-----------------|
| Dunne et al.  | 2014 | UK      | 197      | Hepatectomy     | Retrospective| Cycle Ergo  | Morbidity, LOS  |
| Kaibori et al.| 2013 | Japan   | 61       | Hepatectomy, HCC| Retrospective| Cycle Ergo  | Mortality       |
| Kasivisvanathan et al. | 2015 | UK        | 104      | Hepatectomy     | Prospective  | Cycle Ergo  | Morbidity, LOS  |
| Junejo et al. | 2012 | UK      | 94       | Hepatectomy     | Prospective  | Cycle Ergo  | Mortality, Morbidity |
| Aunania et al. | 2012 | UK      | 124      | PD              | Prospective  | Cycle Ergo  | Morbidity, ISGPS fistula |
| Chandrabalan et al. | 2013 | UK        | 100      | PD, TP          | Retrospective| Cycle Ergo  | Mortality, Morbidity, LOS |
| Junejo et al. | 2014 | UK      | 64       | PD              | Prospective  | Cycle Ergo  | Mortality       |
| Ulyett et al. | 2017 | UK      | 172      | Hepatectomy     | Prospective  | Cycle Ergo  | Morbidity (CD)  |
| Snowdon et al.| 2013 | UK      | 389      | HPB             | Prospective  | Cycle Ergo  | Mortality, LOS  |

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Table 5
Summary of the key findings in studies reviewing use of CPET in major HPB surgery.

| Study     | Year | Country | Patients | Age         | Operation            | Mortality                      | Morbidity | LOS | \( \frac{V˙E}{V˙CO₂} \) ratio at AT | AT (mL/kg/min) | Notes                                      |
|-----------|------|---------|----------|-------------|----------------------|--------------------------------|-----------|-----|-----------------------------------|--------------|-------------------------------------------|
| Ausania et al. 2012 UK | 124 | 66 (IQR 37–82) | Pancreaticoduodenectomy | No significant differences observed. | Patients with a lower AT had increased chance of grades A - C pancreatic fistula: AT \( \leq 10.1 \) – 45% Vs 19.2% if AT \( > 10.1 \) (\( p = 0.020 \)); \( OR = 5.79; CI: 1.62–20.63; \) (\( p = 0.007 \)). For any post-operative complication, 70% vs 38.5% (\( p = 0.013 \)). | Peak VeVCO₂ not significant for pancreatic leaks. (\( p = 0.409 \)). | \( \leq 10.1 \) vs \( > 10.1 \) | Additional factors associated with pancreatic leak were: BMI, jaundice history, pre-operative biliary stent and pancreatic duct size. (\( p \leq 0.100 \)) |
| Chandrabalan et al. 2013 UK | 100 | \( \leq 65 \) (n = 47). > 65 (n = 53). | Pancreaticoduodenectomy, Total pancreatectomy | No association with AT (HR 0.77; CI: 0.16–3.61) (\( p = 0.74 \)). Greater incidence of ISGPS Grade A-C Pancreatic Fistula when AT \( \leq 10 \): 35.4% v 16% (\( p = 0.028 \)); Clavien-Dindo grade III-V intra-abdominal abscesses 22.4% vs 7.8% (\( p = 0.042 \)). Low AT associated with prolonged LOS: 20 days vs 14 day (\( p = 0.005 \)); [HR = 1.74; CI: 1.14–2.65]. | V E/V CO₂ of \( \geq 41 \) predicts poor long-term survival (HR 2.05; CI: 1.09–3.86) (\( p = 0.026 \)), 30 day mortality (OR 1.35; CI: 1.03–1.77) (\( p = 0.030 \)) and in-hospital mortality (OR 1.26; CI 1.06–1.53) (\( p = 0.013 \)). No significance for AT or VO₂ max. Mortality. | \( < 10 \) vs \( \geq 10 \) | Patient’s less likely to receive adjuvant therapy if low AT. (HR = 6.30; CI: 1.25–31.75) (\( p = 0.036 \)). |
| Junejo et al. 2014 UK | 64 | 64 (IQR 45–80) | Pancreaticoduodenectomy | V E/V CO₂ of \( \geq 41 \) predicts poor long-term survival (HR 2.05; CI: 1.09–3.86) (\( p = 0.026 \)), 30 day mortality (OR 1.35; CI: 1.03–1.77) (\( p = 0.030 \)) and in-hospital mortality (OR 1.26; CI 1.06–1.53) (\( p = 0.013 \)). | No significant preoperative CPET variable | - | V E/V CO₂ cut off of 41. | - | Neither AT nor V E/V CO₂ at AT were predictive for morbidity or mortality. |
| Dunne et al. 2014 UK | 197 | 70 (64–75) | Hepatectomy | HR at AT as predictor of CD 3/4 complication had OR 1.02 (1.0–1.04). | Patients with a higher VO₂ L min⁻¹ at AT had increased chances of earlier discharge [hazard ratio 2.15 (CI: 1.15–3.98)]. | - | V E/V CO₂ ratio at AT VeVCO₂ at AT for all complications OR 1.02 (CI 0.96, 1.08) (\( p = 0.541 \)) not significant | AT (mL/kg/min) 11.5 mean (SD 2.4)VO₂ at AT OR 1.02 (CI: 0.91–1.15) (\( p = 0.748 \)). | Notes | CPET Morbidity & Mortality |

(continued on next page)
### Table 5 (continued)

| Study                | Year | Country | Patients | Age            | Operation         | Mortality                          | Morbidity                           | LOS | V E/V CO2 ratio at AT | AT (mL/kg/min) | Notes                                                                 |
|---------------------|------|---------|----------|----------------|-------------------|------------------------------------|-------------------------------------|-----|-----------------------|----------------|-----------------------------------------------------------------------|
| Kaibori et al.      | 2013 | Japan   | 61       | 70 (SD = 9)   | Hepatectomy, HCC  | –                                  | Event free survival had a RR of 2.73 coefficient 1.004 with an SE of 0.412 (p = 0.0148) for an AT of ≥11.5 Vs < 11.5 | –   | 1.18–3.89, P = 0.013 | –              | <11.5 vs > 11.5 Maintenance of Child-Pugh class between patients with AT V O2 ≥11.5 and < 11.5 mL/min/kg (p = 0.0464) |
| Kasivisvanathan et al. | 2015 | UK      | 104      | 65 (IQR 55–70)| Hepatectomy       | –                                  | VO2 at AT for predicting morbidity (POMS defined), (OR 1.23, 95% CI 1.02–1.36) | –   | –                     | 32.4 (29.1–37.2) | Higher V O2 AT had an increased chance of early discharge [hazard ratio (HR) 1.37, 95% CI 1.13–1.58] for POMS >1 (OR 1.02 (.95–1.07)(p = 0.542) |
| Junejo et al.       | 2012 | UK      | 94       | 71 (24–85)    | Hepatectomy       | HR 1.81 (CI 1.04–3.17) for mortality in those with AT <9.9 (p = 0.038) | V E/V CO2 of 34.5 or more at AT to be the only independent predictor (OR 3.97, 95% c.i. 1.44 to 10.96; P = 0.008) | –   | –                     | –              | <9.9 Vs > 9.9                                                                 |
| Ulyett et al.       | 2017 | UK      | 172      | 69 (22–90)    | Hepatectomy       | –                                  | VEqCO2 at AT for developing CD 3/4 OR 1.09 (CI 1.01–1.17) (p = 0.04) (Median VEqCO2 CD0-II versus CDIII-IV 29.1 vs 31.7) vs 31.7 (p = 0.005) | –   | –                     | –              | Mean AT 12.8 (6.4–22.9) versus 12.5 (5.6–23.1) (p = 0.84) |
| Snowdon et al.      | 2013 | UK      | 389      | 66 (SD = 10.3)| HPB               | AT was independent predictor of mortality OR 0.52 (p = 0.003) | Patients with an AT < 10 mL/kg/min spent longer in hospital y2 = 34.9; P < 0.001 | –   | –                     | –              | AT <10 vs > 10 mL/kg/min                                                                 |

**Notes:**
- Event free survival had a RR of 2.73 coefficient 1.004 with an SE of 0.412 (p = 0.0148) for an AT of ≥11.5 Vs < 11.5
- VO2 at AT for predicting morbidity (POMS defined), (OR 1.23, 95% CI 1.02–1.36)
- V E/V CO2 of 34.5 or more at AT to be the only independent predictor (OR 3.97, 95% c.i. 1.44 to 10.96; P = 0.008)
- VEqCO2 at AT for developing CD 3/4 OR 1.09 (CI 1.01–1.17) (p = 0.04)
- V E/V CO2 at AT was not predictive of mortality mean 35.4 (6.1) survivors 35.4 (6.2) versus in patient mortality 36.3 (4.7)(p = 0.55)

**Mean AT (mL/kg/min):**
- 12.8 (6.4–22.9) versus 12.5 (5.6–23.1) (p = 0.84)
in assessing operative suitability, but it also highlights the need for the integration of dynamic parameters from CPET, such as AT and VE/VCO₂ with indices extracted from (P)-POSSUM, alongside other HPB relevant markers when assessing a patient's suitability for major surgery. As clinicians we need to enable patients to make informed decisions regarding their surgical management. Although both tools reviewed are currently in use neither offers sufficiently high predictive power of clinical outcomes to enable a truly informed process. Ultimately, senior clinicians make a decision regarding what they feel is appropriate for an individual patient. Although, this may be informed by years of practice it remains somewhat subjective. A new approach that integrates parameters from both CPET and POSSUM could improve the accuracy of risk stratification and prediction of morbidity and mortality for HPB patients and thus enable a more informed discussion with patients.

5. Conclusion

This review demonstrates the lack of predictive fit of POSSUM and its P-POSSUM derivative al.e in major HPB surgery. We also found that the Anaerobic threshold (AT) provided some predictive power for both morbidity and mortality; an AT cut-off value 10–10.1 ml kg⁻¹ min⁻¹ is likely to be predictive of morbidity after pancreatic surgery, and AT cut-off value of 9.9–11.5 ml kg⁻¹ min⁻¹ is likely to be predictive of post- hepatic surgery complications. However, there are limitations to both the risk estimation tools evaluated and further prospective research looking at how pre-operative static parameters and dynamic physiological variables can be integrated to enable better risk estimation for a group of patients in whom post-operative morbidity is known to be high.

Ethical approval

N/A.

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Author contribution

The study idea, design and conception as well as clinical expertise and advice was provided by VSY, HMK, AA, SB, SH, NM, DH and RH. VDB and JD performed the screening of titles and abstracts, VSY resolved any disagreements as a third independent reviewer. Writing of the review was performed by JD, MZ, VDB and VSY with additional editing and changes by HMK, AA, SB, SH, NM, DH and RH.

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Data statement

All data is accessible on request.

Declaration of competing interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2020.12.016.

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