

Myosteatosi s as a Prognostic Marker for Postoperative Mortality in Adult Patients Undergoing Surgery in General—A Systematic Review

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Abstract: Background: Assessing frailty is important in treating surgical patients to predict peri- and postoperative events like complications or mortality. The current standard is not optimal; therefore, new prognostic markers are being evaluated to enrich the current frailty assessment. One of these new markers is fat degeneration of the psoas muscle (myosteatosi s). This can be assessed by measuring the psoas muscle density (PMD) with computed tomography (CT). The aim of this review is to investigate PMD, and, thus, myosteatosi s, as a prognostic marker for postoperative mortality in adult patients undergoing general surgery. Methods: An electronic search was performed in PubMed to identify relevant studies associating PMD with postoperative mortality. The looked-upon period for mortality to occur did not matter for this review. The looked-upon outcome measure for this review was the hazard ratio. Results: From 659 potential articles from PubMed, 12 were included, for a total of 4834 participants. Articles were excluded when not focused on PMD, if the type of intervention was not specified, and when imaging other than with CT on the level of the third vertebra was performed. The included articles were assessed for bias with the Newcastle–Ottawa Scale (NOS). PMD was, after multivariable analyses, identified as an independent significant prognostic marker for several surgical cardiovascular interventions when we looked at the 5-year mortality rate and for fenestrated branched endovascular aortic repair (F-BEVAR) a slight significant protective correlation between postoperative mortality and PMD (when divided by psoas muscle area (PMI)) when we looked at the 30-day and 3-year mortality. Also, PMD was identified as an independent significant prognostic marker for a variety of surgical gastrointestinal interventions when we looked at 30-day/90-day/1-year/3-year/5-year mortality. PMD was not identified as a significant prognostic marker in urologic surgery. Conclusion: Myosteatosi s has the potential to be a valuable contribution to the current frailty assessment for patients undergoing cardiovascular, gastrointestinal, or urologic surgery. However, more research must be conducted to further strengthen the prognostic value of myosteatosi s, with special attention to, e.g., gender- or age-specific interpretations of the results.

Keywords: myosteatosi s; postoperative mortality; prognostic marker; frailty; psoas muscle density

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1. Introduction

Preoperative frailty assessment is usually performed before any surgery to assess the overall health and risk factors of patients. There are multiple types of assessment used, like the modified frailty index (mFI) or the Charlson co-morbidity index (CCI). Lacking a gold standard, surgeons rely on the patient’s cognition, co-morbidities, body mass index, and physical functioning to adjust the intervention for individual patients with the goal to reduce the risk of complications [1]. This assessment is important because health insurance reimbursements are often reliant on these preoperative frailty assessments [2]. Preoperative frailty assessment used in day-to-day practise is known to be flawed because it is mostly subjective, so new factors or prognostic markers are needed to provide better healthcare

and to improve the healthcare system [3]. The infiltration of adipose depots into skeletal muscle (myosteatorsis) is a potential additional marker for frailty assessment. Myosteatorsis is defined as the infiltration of adipose depots (fat) into skeletal muscle [4]. Specifically, myosteatorsis of the psoas muscle can be evaluated with a CT scan at the L3 vertebra level. Because of its role in posture, stability, and movement, psoas muscle assessment can add information about a patient's mobility, activity, and lifestyle when assessing preoperative frailty [5,6]. Because of the fat infiltration, X-rays from the CT scanner will experience less resistance when passing through the psoas muscle, resulting in a darker tone on the final image. Small changes are not clearly visible on the scan, but new technologies are able to quantify the intensity of the X-rays. This can be expressed in Hounsfield units (HUs). Adipose tissue has an average attenuation of -30 to -70 HUs, whereas healthy muscle has an attenuation of $+10$ to $+40$ HUs [7]. Myosteatorsis happens naturally but increases significantly with age and has a negative correlation with muscle mass, strength, mobility, and disruptive metabolism, and is, for example, linked with disease progression in bowel cancer [8]. Low psoas muscle attenuation can therefore be of clinical value when assessing a patient's preoperative frailty. Until now, sarcopenia (defined as loss of muscle mass) was looked upon as a prognostic variable for postoperative events, but studies suggest no relation between sarcopenia and adverse events [9,10]. Therefore, the goal of this systematic review is to evaluate the prognostic value of psoas muscle density, and, thus, myosteatorsis, on the postoperative mortality of adult patients undergoing general surgery.

2. Methods

2.1. Protocol Registration

The study protocol is registered as PROSPERO under the ID 467197 [11]. For this review, the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines were followed [12]. An overview of these guidelines can be found in Appendix C.

2.2. Search Strategy

A literature search was conducted in the electronic database PubMed on all research work based on myosteatorsis combined with postoperative mortality. No filters, except for an English-only filter, were applied during the search to prevent missing eligible articles. No restriction on the publication period was applied, considering that myosteatorsis is a relatively new topic of interest in frailty assessment research. The keywords of MeSH (Medical Subject Heading) used during the search were 'Adipose tissue', 'lipids', 'adipocytes', 'myostatin', 'psoas muscle', 'postoperative period', 'postoperative complication', 'postoperative care', 'mortality', 'computed tomography, xray', 'diagnostic imaging', 'medical imaging'. The complete search was enriched with free text terms for title and/or abstract to conduct the search as broadly as possible. The complete search query can be found in Appendix A. The articles reviewed were extracted from PubMed on 21 November 2022 exclusively by O.E. den Os and processed with Rayyan.ai. Citation software (EndNote20.1) facilitated the search process to keep a good overview of the references.

2.3. Eligible Criteria

The studies that were considered for this review were required to investigate the role of psoas muscle density, measured with CT on the level of the third vertebra, as a prognostic factor for postoperative mortality in patients undergoing surgery. Assessment of a different muscle, employment of a different imaging technique, or not investigating mortality as an outcome measure and looking at the role of PMD in non-surgical patients resulted in exclusion of the article. The looked-upon outcome for this review was the mortality hazard ratio (HR) at any point postoperative. The HR must be analysed with a multivariable analysis to determine whether it is an independent variable and to get an idea about the effect size of the findings. Missing multivariable analysis of HR resulted in exclusion of the article.

2.4. Data Extraction and Study Interpretation

The following data were extracted from the eligible articles: (i) author and date, (ii) objective, (iii) focus area, (iv) patients' characteristics and numbers, (v) type of surgery investigated in the article, (vi) calculation of psoas muscle density, (vii) results regarding any type of postoperative mortality, and (viii) statistical outcomes. The data were extracted using structured data extraction sheets designed for this study and entered into a secure database.

2.5. Quality Evaluation

The included papers were assessed for their quality. Because of the nature of the studies (retrospective cohort studies) the Newcastle–Ottawa Scale (NOS) was used for the assessment. The NOS is specially designed for assessing the quality of non-randomized studies used for systematic reviews or meta-analyses. There are 3 main criteria, with sub-criteria included: (i) selection, (ii) comparability, and (iii) outcome. These criteria account for 4, 2, and 3 points, respectively, to make a maximum of 9 points. Further explanation of the NOS sub-criteria is provided in Appendix B.

3. Results

3.1. Search Results

The search in PubMed identified 666 potential articles from the existing published literature. After removing the duplicates with Rayyan, 659 articles were screened on title and abstract by O.E. den Os. This excluded 615 articles. These articles were mainly excluded because they focused on psoas muscle mass/area/volume instead of density/attenuation. The remaining 44 articles were full-text screened, resulting in the exclusion of another 32 articles because of wrong methodology, focus on wrong outcome measures, or because they were not available for full-text screening. In total, twelve articles were selected that were relevant and fulfilled the study eligibility criteria. Due to limited suitable articles, no restrictions on study size were applied. Figure 1 gives a summary of the performed search.

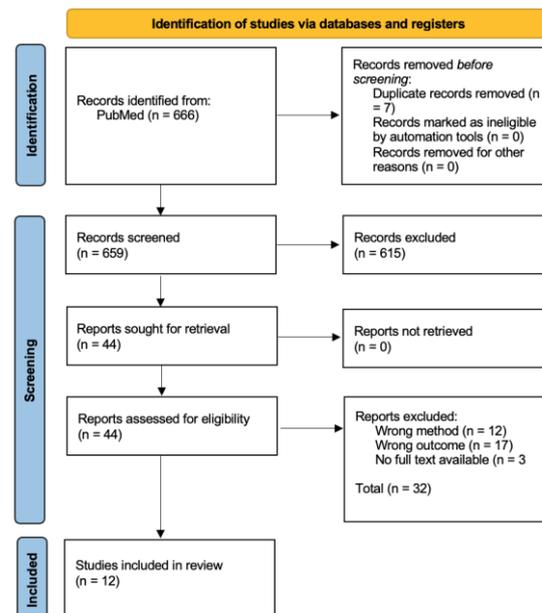


Figure 1. PRISMA flow diagram of the study [12].

3.2. Study Characteristics

The data from the 12 articles were manually extracted by O.E. den Os and visualised using Microsoft Office 2021. To summarize the content of Table 1, of the twelve articles included, three were focused on cardiovascular surgery (Kärkkäinen, 2020 [13]; Yamashita,

2020 [14]; Kärkkäinen, 2021 [15]), eight on gastrointestinal surgery (Lo, 2018 [16]; Salem, 2021 [17]; Miao, 2022 [18]; Herrod, 2019 [19]; Chakedis, 2018 [20]; Wu, 2022 [21]; Uyeda, 2022 [22]; Buettner, 2016 [23]), and one on urology (Yamashita, 2020 [24]). A total of 4582 patients are included. The mean age of this population was 67.91 years and 60.13% of the population was male. The follow-up window for mortality outcomes investigated ranged from 30 days to 5 years. All articles are retrospective cohort studies of patients who initially underwent the investigated intervention. All included studies calculated the density of the psoas muscle according to the Hounsfield Unit Average Calculation (HUAC) method at the L3 vertebra [25]. In all articles, this resulted in two (or three) subgroups based on PMD. Different methods for establishing the optimal cut-off value were used across the included articles, such as 25th percentile, ROC, Cox regression hazard ratio models, median psoas muscle density value, Youden index, and sensitivity analysis. See Table 1.

3.3. Quality Assessment

To assess the quality of the included studies, the NOS was used. Because of the retrospective nature of the included studies and mortality as an outcome, the selection criteria of patients were fitting for all 12 articles and no missing data occurred. The comparability criteria consisted of the comparability of co-morbidities (modified frailty index (mFI) [26] or Charlson co-morbidity index (CCI) [27]) and type of intervention between the defined groups. Lo, 2018 [16]; Herrod, 2019 [19]; Chakedis, 2018 [20]; and Miao, 2022 [18] failed to meet one of the two criteria. The last criterion consisted of specifics of the outcome measure. Yamashita, 2020 [14] was the only article that specified the adequacy of the follow-up period. A summary of the results is displayed in Table 2, and the full quality assessment is added in Appendix B.

3.4. Individual Results

All studies except Lo, 2018 [16] presented a multivariable analysis. These analyses were done to identify psoas muscle density as an independent prognostic marker for postoperative mortality. Between the three focus areas (cardiovascular, gastrointestinal, and urological), the cut-off value for low density and high density varied. Kärkkäinen, 2020 [13] and Kärkkäinen, 2021 [15] even divided the PMD by the psoas muscle index (PMI), which resulted in a cut-off value that was not comparable with the other articles. The average cut-off value (not gender-specific) for low PMD was ≤ 34.2 HU (so >34.2 HU was high PMD). Miao, 2022 [18]; Wu, 2022 [21]; Uyeda, 2022 [22]; and Buettner, 2016 [23] identified different cut-off values for males and females. The other articles did not differentiate between genders in determining cut-off points. See Table 3 for more detailed information.

3.4.1. Cardiovascular Surgery

Three of the included articles focused on cardiovascular surgery. Yamashita, 2020 [14] found a significant HR (2.42 (1.32–4.45), $p = 0.004$) indicating psoas muscle density as an independent prognostic predictor for 5-year mortality in a variety of cardiovascular surgical interventions. Kärkkäinen, 2020 [13] and Kärkkäinen, 2021 [15] only explored PMD divided by PMI as a prognostic variable for fenestrated branched endovascular aortic repair and found a significant hazard ratio (0.998 (0.990–0.998), 0.998 (0.997–0.999) resp.) for 90-day and 3-year mortality.

Table 1. Study characteristics of the 12 included articles. This table displays the study size, the objective of the study, the type of intervention that was performed, which mortality outcome measure was taken into consideration, what kind of patient was included in the study, and what method was used to determine the cut-off value for high and low psoas muscle density. All the above-mentioned studies were retrospective cohort studies found on PubMed. SMD = skeletal muscle density.

Author	Study Size (M/F)	Objective	Type of Intervention	Mortality	Data Sources	Method for Determining Cut-Off Value for High and Low Psoas Muscle Density
Kärkkäinen (2020) [13]	244 (172/72)	To investigate the association between psoas muscle area (PMA) and density (PMD) with survival and quality of life (QoL) after fenestrated branched endovascular aortic repair (F-BEVAR).	Fenestrated branched endovascular aortic repair (F-BEVAR)	30-day, 90-day	Patients undergoing F-BEVAR operation between November 2013 and March 2018.	Cox regression hazard ratio models with splines for association with time-dependent mortality
Yamashita (2020) [14]	1068 (679/389)	To determine the preoperative SMD cut-off using the psoas muscle and to investigate the effect on postoperative outcomes, including sarcopenia, in cardiovascular patients.	Coronary artery bypass grafting, valve, aorta, congenital, tumour/thrombus, multiple, other	5-year	Patients who underwent cardiovascular surgery and participated in cardiac rehabilitation at least once between 1 January 2008 and 31 December 2017.	Youden index
Kärkkäinen (2021) [15]	504 (371/133)	To evaluate the psoas muscle area and attenuation (radiodensity), quantified by computed tomography, together with clinical risk assessment, as predictors of outcomes after fenestrated branched endovascular aortic repair (F-BEVAR).	Fenestrated branched endovascular aortic repair (F-BEVAR)	30-day, 3-year	Patients who had undergone elective F-BEVAR for pararenal or thoracoabdominal aortic aneurysms.	Cox regression hazard ratio models with splines for association with time-dependent mortality
Lo (2018) [16]	100 (46/54)	To evaluate CT-based psoas muscle density as a prognostic marker for poor outcomes after ECF repair.	Enterocutaneous fistula repair (ECF)	90-day, 1-year, 3-year	Patients who, between 2005 and 2015, underwent ECF repair comprising laparotomy, en bloc overlying of skin with bowel resection and anastomosis that had a CT scan of abdomen/pelvis with venous contrast within three months before operative repair.	25th percentile (IQR1)
Salem (2021) [17]	383 (122/161)	The hypothesis was that in elderly patients undergoing EL, these easily measured sarcopenia parameters are independent risk factors of mortality and poor postoperative course.	Peritonitis, hernia, obstruction, ischemia, perforation, other indication	30-day	Patients aged >65 yr who were admitted to the emergency department and required emergency laparotomies between 2006 and 2011.	25th percentile (IQR1)

Table 1. Cont.

Author	Study Size (M/F)	Objective	Type of Intervention	Mortality	Data Sources	Method for Determining Cut-Off Value for High and Low Psoas Muscle Density
Miao (2022) [18]	88 (75/13)	To investigate the association between PMD and short-term postoperative outcomes in patients with acute mesenteric ischemia (AMI).	Revascularisation with or without resection of the mesentery	30-day	Patients who underwent surgical intervention by revascularization with or without resection and had abdominal non-contrast CT scans before surgery.	25th percentile (IQR1)
Herrod (2019) [19]	169 (91/78)	To assess the association between radiologically defined sarcopenia measured by psoas density and postoperative outcomes in patients having a colorectal cancer resection.	Colorectal cancer resection, anterior resection, right hemicolectomy, abdominoperineal excision of rectum, extended right hemicolectomy, subtotal/pan proctocolectomy, Hartmann's resection	90-day, 1-year	Patients having a resection for colorectal cancer, discussed by the colorectal multi-disciplinary team in one institution in 2015.	Receiver-operator curve (ROC)
Chakedis (2018) [20]	117 (52/65)	To define the impact of sarcopenia on survival among patients undergoing resection of BTC.	Laparoscopy/laparotomy, pancreaticoduodenectomy, partial hepatectomy, R hepatectomy +/- bile duct, L hepatectomy +/- bile duct, radical cholecystectomy, extrahepatic BD resection, cholecystectomy	30-day, 1-year	Patients who underwent exploration for BTC who had a preoperative CT scan available for review were identified between 2007 and 2016.	Log rank statistics and ROC
Wu (2022) [21]	228 (138/90)	To verify the universality of the conclusion that sarcopenia affected the prognosis of emergency laparotomy in a different population setting.	Perforation repairment, appendectomy, adhesiolysis, exploratory, abdominal hernia, reduction of volvulus, drainage of abscess, small bowel resection, colon colostomy, right colectomy, left colectomy, other colorectal resection, Harmann's, removal of foreign body, other tumour resection, gastrectomy, enterostomy, resection of Meckel's diverticulum	30-day	Patients who underwent emergency laparotomy from 1 September 2019 to 31 August 2021.	Not clearly defined in article

Table 1. Cont.

Author	Study Size (M/F)	Objective	Type of Intervention	Mortality	Data Sources	Method for Determining Cut-Off Value for High and Low Psoas Muscle Density
Uyeda (2022) [22]	297 (127/170)	To describe five different CT methods of measuring sarcopenia and muscle quality and to determine which method has the greatest sensitivity for predicting 1-year mortality following emergency abdominal surgery in elderly patients.	Gastrointestinal resection, cholecystectomy, hernia repair, laparotomy with adhesiolysis only, appendectomy, palliative stoma for malignance, repair of perforated peptic ulcers, intestinal bypass for malignancy, mesenteric revascularization	30-day, 60-day, 90-day, 1-year	Patients 70 years and older who underwent 'urgent' or 'emergent' laparotomy or laparoscopy for acute abdominal disease between 2006 and 2011.	25th percentile (IQR1)
Buettner (2016) [23]	1326 (730/596)	To develop a preoperative frailty-risk model combining sarcopenia with clinical parameters to predict 1-year mortality using a cohort of patients undergoing gastrointestinal cancer surgery.	Hepatectomy, pancreatectomy, colorectal resection	1-year	Patients undergoing hepatobiliary, pancreatic, or colorectal surgery between 2011 and 2014.	Sensitivity analysis
Yamashita (2020) [24]	230 (184/46)	This study aimed to evaluate the influence of myosteatorsis on survival of patients after radical cystectomy (RC) for bladder cancer.	Open/laparoscopic/robotic approach, with either ileal conduit or cutaneous ureterostomy	2-year	Patients who underwent RC for bladder cancer at our three institutions between 2009 and 2018	Median of average total psoas density

Table 2. Newcastle–Ottawa Scale assessment of the 12 included articles. Full analysis available in Appendix B.

Author	Selection (4)	Comparability (2)	Outcome (3)	Total (9)
Kärkkäinen (2020) [13]	4	2	2	8
Yamashita (2020) [14]	4	2	2	8
Kärkkäinen (2021) [15]	4	2	2	8
Lo (2018) [16]	4	1	2	7
Salem (2021) [17]	4	2	2	8
Miao (2022) [18]	4	1	2	7
Herrod (2019) [19]	4	1	2	7
Chakedis (2018) [20]	4	1	2	7
Wu (2022) [21]	4	2	2	8
Uyeda (2022) [22]	4	2	2	8
Buettner (2016) [23]	4	2	2	8
Yamashita (2020) [24]	4	2	3	9

3.4.2. Gastrointestinal Surgery

Eight articles were included with a focus on postoperative mortality in gastrointestinal surgery. As seen in Table 1, a vast range of surgical interventions and follow-up periods were investigated. However, not all articles reckoned their groups for the intervention as seen in Table 2. Only Herrod, 2019 [19] and Wu, 2022 [21] did not find a significant outcome for 1-year and 30-day mortality, respectively (1.73 (0.47–6.3), $p = 0.406$; 2.256 (0.885–5.748), $p = 0.088$ resp.). Salem, 2021 [17]; Miao, 2022 [18]; and Uyeda, 2022 [22] did find significant conclusive 30-day mortality outcomes (2.35 (1.16–4.76), $p = 0.017$; 10.667 (2.450–46.436), $p = 0.002$; 2.7 (1.3–5.4), $p = 0.006$), see Table 4. The found hazard ratios were combined according to a fixed model meta-analysis, resulting in an overall effect of 3.148 (1.245–9.020). Uyeda, 2022 [22] also reported a significant HR for 90-day mortality (2.4 (1.4–4.2), $p = 0.003$) and 1-year mortality 2.1 ((1.3–3.3), $p = 0.001$). Likewise, Buettner, 2016 [23] calculated that the HR for 1-year mortality in gastrointestinal surgery was 1.98 ((1.36–2.88), $p = < 0.001$). Lastly, Lo, 2018 [16] found significant 1-year and 3-year mortality likelihood ratios (7.79 (1.57–38.57), $p = 0.01$; 22.37 (3.07–162.95), $p = < 0.01$ resp.). The 1-year mortality HRs are displayed in Table 5, and a fixed model meta-analysis was performed, resulting in an overall effect of 1.977 (1.266–3.254).

3.4.3. Urologic Surgery

Yamashita, 2020 [14] was the only paper that was included focusing on urologic surgery. There was no significant correlation between PMD and postoperative mortality when we looked at a 2-year mortality period.

Table 3. Results of the 12 included articles. Significance was determined at $p \leq 0.05$. The (-) indicate that those results were not mentioned in the article, or that the article did not look at that outcome measure. All HRs were determined in a multivariable analysis. (HUs) = Hounsfield units. (*) Outcome is cm2HU instead of HU. The PMD is divided by PMI. (**) HR for 2-year mortality instead of 1-year mortality. (M) indicates cut-off point for male and (F) for female.

Author	Cut-Off Point (HU)			Number of Patients			HR (CI 95%)					Likelihood Ratio				
	Low	Medium	High	Total (M/F)	Low HU	Medium HU	High HU	30 Days	90 Days	1 Year	3 Years	5 Years	p-Value	1 Year	3 Years	p-Value
Kärkkäinen (2020) [13]	<200 *	200–350 *	>350 *	504 (371/133)	33	181	290	-	0.994 (0.990–0.998)	-	-	-	0.003	-	-	-
Yamashita (2020) [14]	<45	-	≥45	1068 (679/389)	551	-	517	-	-	-	-	2.42 (1.32–4.45)	0.004	-	-	-
Kärkkäinen (2021) [15]	≤350 *	-	>350 *	224 (172/72)	165	-	79	-	-	-	0.998 (0.997–0.999)	-	0.001	-	-	-
Lo (2018) [16]	≤32.6	-	>32.6	100 (46/54)	25	-	75	-	-	-	-	-	-	7.79 (1.57–38.57)	22.37 (3.07–162.95)	0.01/<0.01
Salem (2021) [17]	≤35.5	-	>35.5	283 (122/161)	73	-	210	2.35 (1.16–4.76)	-	-	-	-	0.017	-	-	-
Miao (2022) [18]	≤40.5(M)/28.4(F)	-	>40.5 (M)/28.4 (F)	88 (75/13)	21	-	67	10.667 (2.450–46.436)	-	-	-	-	0.002	-	-	-
Herrod (2019) [19]	≤44.5	-	>44.5	169 (91/78)	51	-	118	-	-	1.73 (0.47–6.3)	-	-	0.406	-	-	-
Chakedis (2018) [20]	≤38	-	>38	117 (52/65)	-	-	-	-	-	-	-	2.96 (1.21–7.21)	0.017	-	-	-
Wu (2022) [21]	≤34.9(M)/27.8(F)	-	>34.9 (M)/27.8 (F)	228 (138/90)	56	-	171	2.256 (0.885–5.748)	-	-	-	-	0.088	-	-	-
Uyeda (2022) [22]	≤23.9(M)/26.6(F)	-	>23.9 (M)/26.6(F)	297 (127/170)	75	-	222	2.7 (1.3–5.4)	2.4 (1.4–4.2)	2.1 (1.3–3.3)	-	-	0.006/0.003/0.001	-	-	-
Buettner (2016) [23]	≤39.9(M)/38.1(F)	-	>39.9 (M)/38.1(F)	1326 (730/596)	398	-	928	-	-	1.98 (1.36–2.88)	-	-	<0.001	-	-	-
Yamashita (2020) [24]	<44	-	≥44	230 (184/46)	67	-	163	-	-	0.98 ** (0.95–1.00)	-	-	0.18	-	-	-

Table 4. Forest plot displaying 30-day mortality hazard ratio (Uyeda, 2022 [22]; Wu, 2022 [21]; Miao, 2022 [18]; and Salem, 2021 [17]) and overall effect according to fixed model meta-analysis for low-PMD patients undergoing gastrointestinal surgery.

Study	Study Size	Hazard Ratio (95% CI)	Weight (%)	HR (95% CI)
Miao (2022) [18]	88		9.82	10.667 (2.450–46.436)
Uyeda (2022) [22]	297		33.15	2.7 (1.3–5.4)
Salem (2021) [17]	283		31.58	2.35 (1.16–4.76)
Wu (2022) [21]	228		25.45	2.256 (0.885–5.748)
Overall effect	896		100	3.148 (1.245–9.020)

Table 5. Forest plot displaying 1-year mortality hazard ratio (Buettner, 2016 [23]; Uyeda, 2022 [22]; Herrod, 2019 [19]) and overall effect according to fixed model meta-analysis for low-PMD patients undergoing gastrointestinal surgery.

Study	Study Size	Hazard Ratio (95% CI)	Weight (%)	HR (95% CI)
Uyeda (2022) [22]	297		16.57	2.1 (1.3–3.3)
Buettner (2016) [23]	1326		74.0	1.98 (1.36–2.88)
Herrod (2019) [19]	169		9.43	1.73 (0.47–6.30)
Overall effect	1792		100	1.977 (1.266–3.254)

4. Discussion

4.1. Summary of Results

This systematic literature review was conducted to evaluate if psoas muscle density could be a prognostic marker for postoperative mortality in patients undergoing general surgery. In total, twelve papers were included and analysed with the purpose of creating better preoperative frailty assessment. The articles covered three branches of surgery: cardiovascular surgery, gastrointestinal surgery, and urologic surgery. These subgroups have three, eight, and one article, respectively, and will be discussed separately for better comparison of the results.

4.1.1. Cardiovascular Surgery

The three included studies focussing on cardiovascular interventions are hard to compare because Kärkkäinen, 2020 [13] and Kärkkäinen, 2021 [15] used a different unit for PMD (PMD divided by PMI) and focused only on F-BEVAR when compared to Yamashita, 2020 [14]. The found hazard ratio in both Kärkkäinen, 2020 [13] and Kärkkäinen, 2021 [15] is not strong (0.998 (0.990–0.998), 0.998 (0.997–0.999) resp.), but it is significant when looked

at over a 90-day and 3-year period. However, the correlation between PMD and PMI in those two studies is not clear, making it difficult to interpret the found hazard ratios when assessing the correlation between PMD and postoperative mortality. Yamashita, 2020 [14] found a strong correlation between PMD and postoperative mortality when looking at a period of 5 years (2.42 (1.32–4.45)). The slightly different PMD measurement techniques complicate the predictive value of myosteatorosis as a prognostic marker for postoperative mortality in cardiovascular surgery and raises the question of which method is most suitable to further investigate.

4.1.2. Gastrointestinal Surgery

The findings of the eight articles focused on gastrointestinal interventions suggest a correlation between PMD and mortality because of the favourable HRs. Uyeda, 2022 [22]; Chakedis, 2018 [20]; Salem, 2021 [17]; Buettner, 2016 [23]; and Lo, 2018 [16] found a meaningful correlation between PMD and 30-day, 90-day, 1-year, and 3-year postoperative mortality. They found significant HRs and likelihood ratios with confidence intervals that do not contain one. This indicates a true correlation between PMD and postoperative mortality. Even though Miao did find promising outcomes, their claim to find a correlation is weakened by the fact that only 88 patients were included and because the confidence interval is very wide. More patients must be evaluated to validate these findings. The other two articles did not find a correlation between PMD and mortality. A reason for Herrod, 2019 [19] not finding a correlation could be the relatively high cut-off value (44.5 vs. 34.2 (average)). This is not further specified in their article.

4.1.3. Urologic Surgery

One paper, Yamashita, 2020 [24], was included regarding urologic surgery. This paper found no significant indication that PMD had a negative effect on 2-year mortality (HR 0.98 (0.95–1.00), $p = 0.18$) in patients undergoing an open, laparoscopic, or robotic approach, with either ileal conduit or cutaneous ureterostomy. Even though this article presents concessive outcomes, more investigation needs to be conducted to strengthen the correlation between PMD and postoperative mortality in urologic surgery, and also to assess different urological interventions that could benefit from this promising prognostic marker.

4.2. Discussion

4.2.1. Limitations of Articles

Some limitations regarding the investigated articles exist. First, the comparability between the different articles is not optimal due to the heterogeneity of interventions used and follow-up period of mortality outcomes. Second, the cut-off value for low/medium/high PMD is different between the articles. Even though the cut-off range is similar, some articles also differentiate between male and female cut-off points, while other articles use a single cut-off point for all participants. As a result, the useability of the found HRs varies, making it difficult to determine the optimal cut-off point for PMD as a prognostic marker for postoperative mortality. Third, especially for cardiovascular and urologic surgery, there is a lack of available literature regarding PMD as a prognostic marker for postoperative mortality. Fourth, not all articles took the difference between interventions into account. This creates indistinctness of the relation between PMD and procedure-specific postoperative mortality. Fifth, the average age of the population is 67.91 years. This is not representative of all patients undergoing surgery. This all makes it hard to generalize these outcomes for day-to-day clinical application. Therefore, more research needs to be conducted to (i) find an optimal cut-off point for high and low PMD for different subsets like gender and age, and (ii) to strengthen the here-found relation between PMD and (procedure-specific) postoperative mortality.

4.2.2. Limitations Review

The limitations of this review are that the selection of articles and the extraction of the data were conducted solely by O.E. den Os. This could cause observation bias in selecting articles, extracting data, and in the interpretation of the results. Also, only PubMed was explored for eligible articles. For further (systematic) studies, different databases such as Cochrane, WebMD, Google Scholar, or Web of Science must be searched for eligible articles, and a second, and preferably a third, analyst should be instated to assure objectivity in study selection, data extraction, and interpretation of the results. Another factor that must be considered is that this field of research is relatively new and, therefore, new articles and insights can be published between the time the search was conducted (28 November 2022) and the date of publication of this article.

5. Conclusions

This systematic literature review concludes that PMD has the potential to be an independent prognostic marker for postoperative mortality in cardiovascular, gastrointestinal, and urologic surgery. However, (gender- and age-) specific cut-off points and measurement methods must be determined before they can be of clinical value. Also, more research must be conducted to further strengthen the position of PMD as a prognostic marker for postoperative mortality in cardiovascular, gastrointestinal, and urologic surgery. Furthermore, other regions of surgery in addition to cardiovascular, gastrointestinal, and urologic surgery should be investigated to determine the role of PMD as an addition for frailty assessment in patients undergoing surgery. This systematic review has focussed on the correlation between PMD and postoperative mortality. Another vital step for implementing PMD as an addition to the current frailty assessment is to investigate the prognostic value of PMD on peri- and/or postoperative complications.

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Data Availability Statement: Data is contained within the article.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Table A1. Number of articles on PubMed for individual and combined search terms used.

Search	Entry Terms	Hits
#1	myosteato*(tiab)	327 results
#2	intermuscular adipose tiss*(tiab)	256 results
#3	intramuscular adipose tiss*(tiab)	322 results
#4	intramyocellular lipid*(tiab)	757 results
#5	muscle fat(tiab)	1499 results
#6	fat accumulat*(tiab)	7554 results
#7	fat infiltrat*(tiab)	1245 results
#8	lipid* infiltration(tiab)	6449 results
#9	lipid infiltrat* (tiab)	323 results
#10	lipid accumulat* (tiab)	14,908 results
#11	lipid* accumulation(tiab)	53,474 results
#12	muscle ag*(tiab)	646 results
#13	myostatin(tiab)	3277 results
#14	muscle steatos*(tiab)	18 results
#15	reduced muscle radiodensit*(tiab)	12 results
#16	psoas muscle*(tiab)	2976 results
#17	low muscle attenuat*(tiab)	19 results
#18	intramuscular adiposit*(tiab)	14 results
#19	adipose tissue(MeSH Terms)	109,024 results
#20	lipids(MeSH Terms)	1,260,023 results
#21	adipocytes(MeSH Terms)	26,152 results
#22	myostatin(MeSH Terms)	2200 results
#23	psoas muscle(MeSH Terms)	1985 results
#24	psoas muscles(MeSH Terms)	1985 results
#25	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24	1,400,834 results
#26	postoperative complicat*(tiab)	85,700 results
#27	surgical outcome*(tiab)	30,071 results
#28	surgical*(tiab)	1,189,693 results
#29	mortality (tiab)	948,429 results
#30	adverse effect*(tiab)	190,089 results
#31	adverse event*(tiab)	209,836 results
#32	readmission*(tiab)	40,448 results
#33	infectious complicat*(tiab)	14,991 results
#34	postoperative morbidit*(tiab)	13,221 results
#35	postoperative period(MeSH Terms)	61,408 results
#36	postoperative periods(MeSH Terms)	61,408
#37	postoperative complication(MeSH Terms)	601,607 results
#38	postoperative complications(MeSH Terms)	601,607 results

Table A1. Cont.

Search	Entry Terms	Hits
#39	postoperative care(MeSH Terms)	60,743 results
#40	mortality(MeSH Terms)	421,276 results
#41	#26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40	2,392,845 results
#42	CT*(tiab)	415,646 results
#43	Computed tomograph*(tiab)	333,727 results
#44	medical imag*(tiab)	20,658 results
#45	imag*(tiab)	1,465,548 results
#46	diagnostic imag*(tiab)	21,172 results
#47	computed tomography, x ray(MeSH Terms)	483,482 results
#48	computed tomography, xray(MeSH Terms)	483,482 results
#49	xray computed tomography(MeSH Terms)	483,482 results
#50	diagnostic imaging(MeSH Terms)	2,874,928
#51	medical imaging(MeSH Terms)	2,874,928 results
#52	#42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51	3,750,803 results
#53	psoas muscle*(tiab)	2976 results
#54	psoas(tiab)	6783 results
#55	muscle, psoas(MeSH Terms)	1985 results
#56	psoas muscles(MeSH Terms)	1985 results
#57	#53 OR #54 OR #55 OR #56	7392 results
#58	#25 AND #41 AND #52 AND #57	666 results

Appendix B

Table A2. Full table bias assessment with the Newcastle–Ottawa Scale. (*) The two main criteria for this review were comparability in frailty (mFI and CCI) and intervention type.

Author	Selection (4)				Comparability (2)	Outcome (3)			Total
	Representativeness of the Exposed Cohort (1)	Selection of the Non-Exposed Cohort (1)	Ascertainment of Exposure (1)	Demonstration That Outcome Was Not Present at Start of the Study (1)	Comparability of Cohorts Based on Design and/or Analyses * (2)	Assessment of Outcome (1)	Was the Follow-Up Long Enough for the Outcome to Occur (1)	Adequacy of Follow-Up (1)	
Kärkkäinen (2020) [13]	1	1	1	1	2	1	1	0	8
Yamashita (2020) [14]	1	1	1	1	2	1	1	0	8
Kärkkäinen (2021) [15]	1	1	1	1	2	1	1	0	8
Lo (2018) [16]	1	1	1	1	1	1	1	0	7
Salem (2021) [17]	1	1	1	1	2	1	1	0	8
Miao (2022) [18]	1	1	1	1	0	1	1	0	6
Herrod (2019) [19]	1	1	1	1	1	1	1	0	7
Chakedis (2018) [20]	1	1	1	1	1	1	1	0	7
Wu (2022) [21]	1	1	1	1	2	1	1	0	8
Uyeda (2022) [22]	1	1	1	1	2	1	1	0	8
Buettner (2016) [23]	1	1	1	1	2	1	1	0	8
Yamashita (2020) [24]	1	1	1	1	2	1	1	1	9

Appendix C

Table A3. PRISMA guidelines [10].

Section/Topic	#	Checklist Item	Reported on Page #
Title			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
Methods			
Protocol and registration	5	Indicate if a review protocol exists, and if so, where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2/3
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix A
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	3 and Appendix B
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3
Synthesis of results	14	Describe the methods of handling data and combining results of studies; if done, including measures of consistency (e.g., I^2) for each meta-analysis.	3
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not applicable

Table A3. Cont.

Section/Topic	#	Checklist Item	Reported on Page #
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression); if done, indicating which were pre-specified.	Not applicable
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	3
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary of data for each intervention group; (b) effect estimates and confidence intervals, ideally with a forest plot.	8/9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Not applicable
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression (see Item 16)).	Not applicable
Discussion			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11
Limitations	25	Discuss limitations at study and outcome levels (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	Not applicable

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