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REVIEW

Outcomes of Acute Limb Ischaemia in Patients with Underlying Malignancy: A Systematic Review

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Objective: Previous studies have demonstrated amputation and mortality rates to be 14.3% — 30% and 11.4% — 28.9%, respectively, for all patients presenting with acute limb ischaemia (ALI). Rates of ALI are higher in patients with malignancy than in those without. Despite this, there remains uncertainty with regards to the most appropriate management for patients with cancer presenting with ALI. This is because of previously published high rates of associated morbidity and mortality in this population. The aim of this review was to summarise the available evidence reporting on outcomes of ALI in patients with underlying malignancy.

Method: A systematic review was performed in August 2020 in accordance with the PRISMA guidelines. The Medline, Scopus, Cochrane, and Embase databases were searched with the following search string ((acute limb ischaemia) OR (acute limb ischemia)) AND ((cancer) OR (malignancy)). A total of 849 papers were identified and reviewed; six studies were included. Studies were assessed for bias using the National Institute of Health/ National Heart, Lung and Blood Institute Quality Assessment Tool. Data including demographics, Rutherford classification, baseline performance scores, method of revascularisation, and peri-procedural outcomes were extracted and analysed. Data were pooled based on outcomes of interest and pooled prevalence was reported with 95% confidence intervals (CI).

Results: Six studies with 284 patients with cancer were included for analysis. The pooled overall risk of amputation was 15% (95% CI 5.9 — 26.9). The pooled 30 day mortality rate was 24% (95% CI 14.7 — 34.6).

Conclusion: Despite limitations of interstudy selection bias and some clinical heterogeneity, the included studies demonstrated acceptable short and medium term outcomes for patients with cancer undergoing revascularisation for acute limb ischaemia. This is in line with current recommendations that patients with underlying malignancy should be considered strongly for revascularisation.

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INTRODUCTION

The incidence of acute limb ischaemia (ALI), defined as any sudden decrease in limb perfusion causing a potential threat to limb viability,[1] is 9 — 16 cases per 100 000 persons per year.[2—4] ALI is a vascular emergency associated with substantial morbidity and mortality. Despite advances in the management of ALI, studies looking at all patients presenting to hospital with ALI have demonstrated short term mortality rates between 11.4% and 28.9%[1,5,6] and amputation rates of 14.3% — 30%.[1,5,6] The estimated five year economic cost of ALI is over €24 000 per patient.[7] Although venous thromboembolism is a known consequence of malignancy, the relationship between cancer and acute arterial thromboembolism is less well established,[8] with evidence of increased incidence derived primarily from smaller case series.[8,9] The increased risk of thromboembolic events in patients with cancer is complex and multifactorial; both the underlying disease and systemic treatments lead to a prothrombotic state, exacerbated by tumorigenic inflammatory responses, abnormal protein metabolism, and haemodynamic compromise leading to subsequent stasis.[10]

Previous studies have demonstrated poor outcomes in patients undergoing revascularisation for acute limb ischaemia with underlying malignancy.[8,10,11] Historically, ALI has been considered a terminal event for patients with active malignancy, leading to a preference for a conservative or palliative approach in this patient cohort.[8,10,12,13] However, more recent studies have challenged this viewpoint, observing similar 30 day survival rates to those without malignancy.[9,14] These studies argue for a more nuanced approach, concluding that palliation for this group

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of patients could be justified only in cases of terminal cancer where short term prognosis is poor.[9,14]

Recently updated clinical practice guidelines on the management of acute limb ischaemia published by the European Society for Vascular Surgery (ESVS) 2020 recommended that active revascularisation in selected patients with an underlying malignancy should be considered, as the immediate post-operative outcome is comparable with that of patients without malignancy (Class IIa Level B).[15]

This review examined the available literature from the Medline, Embase, Scopus and Cochrane databases to determine the outcomes for patients with underlying malignancy presenting with ALI.

METHOD

Protocol and information sources

Prior to completion, the protocol for this systematic review was registered with PROSPERO (PROSPERO registration number CRD42020214083). The search was performed in August 2020 in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines[16] using the search string ((acute limb ischaemia) OR (acute limb ischemia)) AND ((cancer) OR (malignancy)). Medline, Embase, Cochrane, and Scopus databases were searched. The search was not language restricted. Unpublished data or abstracts were not included.

Search, eligibility criteria, and study selection

All original articles examining the outcomes of patients with an active underlying malignancy who presented with acute limb ischaemia were included for analysis. After duplicates were removed, titles and abstracts were screened for relevance. Full texts of the remaining studies were obtained. Full text articles were reviewed independently by two reviewers (AK, CT). Decisions regarding article inclusion were resolved by consensus (AK, CT). In cases of disagreement, an external peer was consulted.

Inclusion and exclusion criteria

Articles were screened based on the inclusion and exclusion criteria summarised in Table 1. Full text original articles were eligible for inclusion if they described outcomes of patients with ALI and a concurrent or recently diagnosed cancer. Review articles and case reports were excluded. Case series of 10 or more participants were eligible. Published abstracts and conference proceedings were excluded.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Clinical studies reporting outcomes of acute limb ischaemia in patients with active malignancy	Critical limb ischaemia
	Review articles
	Case reports
Full text available	Cadaveric studies
	Animal studies

Reference lists of included studies were manually searched for relevant studies.

ALI was defined as a sudden decrease in arterial perfusion of the limb, with a potential threat to limb survival, requiring urgent evaluation and management, with symptom duration less than two weeks.[15] Studies reporting solely on critical limb ischaemia were excluded. Papers that looked at patients with a history of cancer and not specifically at patients with currently active cancer were excluded.

Data collection process and data items

Information was extracted from selected articles for the following variables by two independent reviewers (AK, CT): age, gender, Rutherford classification for ALI, method of revascularisation, baseline performance status, primary amputation rate, 30 day amputation rate, and 30 day morbidity and mortality rates.

Risk of bias in individual studies

The quality of the included studies was assessed by two independent investigators (AK, CT) according to the National Institute of Health/National Heart, Lung and Blood Institute (NIH/NHLBI) Quality Assessment Tool for Observational Cohort and Cross Sectional Studies,[17] and is outlined in Table 2.

Summary measures

Continuous variables were reported as weighted mean based on study sample size, while categorical variables were reported as frequencies with percentages. Results were pooled for comparable cohorts and outcome measures.

Synthesis of results and statistical analysis

Statistical analysis was performed using R (R Core Team version 3.7, 2020).[18] Outcome data are reported as the proportion of the patients having the outcome, with 95% confidence intervals generated using an inverse variance random effects model. Heterogeneity was assessed by means of the I^2 statistic, with a value of $>50\%$ considered to indicate statistically significant heterogeneity.

Research ethics

No ethical approval was needed because only data from previous published studies in which informed consent was obtained by primary investigators were included.

RESULTS

Study selection and quality assessment

Fig. 1 is the PRISMA flow diagram. A total of 849 articles were returned on initial database search. Of these, 56 were duplicate results. Six hundred and fifty eight articles were excluded based on title and abstract screening for relevance, and 135 full text articles were assessed for eligibility based on the inclusion and exclusion criteria outlined in

Table 2. Quality of included studies was assessed according to the National Institute of Health/National Heart, Lung and Blood Institute (NIH/NHLBI) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies.

	Silverberg et al.[19]	Mouhayar et al.[14]	Javid et al.[10]	Bennett et al.[13]	Morris-Stiff et al.[8]	Tsang et al.[9]
1. Was the research question or objective in this paper clearly stated?	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the study population clearly specified and defined?	Yes	Yes	Yes	Yes	Yes	Yes
3. Was the participation rate of eligible persons at least 50%?	NR	NR	NR	NR	NR	NR
4. Were all the subjects selected or recruited from the same or similar populations? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Yes	Yes	Yes	Yes	Yes	Yes
5. Was a sample size justification, power description, or variance and effect estimates provided?	NR	NR	NR	NR	NR	NR
6. Were the exposure(s) of interest measured prior to the outcome(s) being measured?	Yes	Yes	Yes	No	No	Yes
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Yes	Yes	Yes	Yes	Yes	Yes
8. Did the study examine different levels of the exposure as related to the outcome?	Yes	Yes	No	No	No	Yes
9. Were the exposure measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes
10. Was the exposure(s) assessed more than once over time?	NA	NA	NA	NA	NA	NA
11. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes	Yes	Yes
12. Were the outcome assessors blinded to the exposure status of participants?	No	No	No	No	No	No
13. Was loss to follow up after baseline 20% or less?	Yes	Yes	Yes	Yes	Yes	Yes
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	Yes	Yes	No	Yes	No	No
Overall Quality Rating	Good	Good	Fair	Good	Fair	Fair

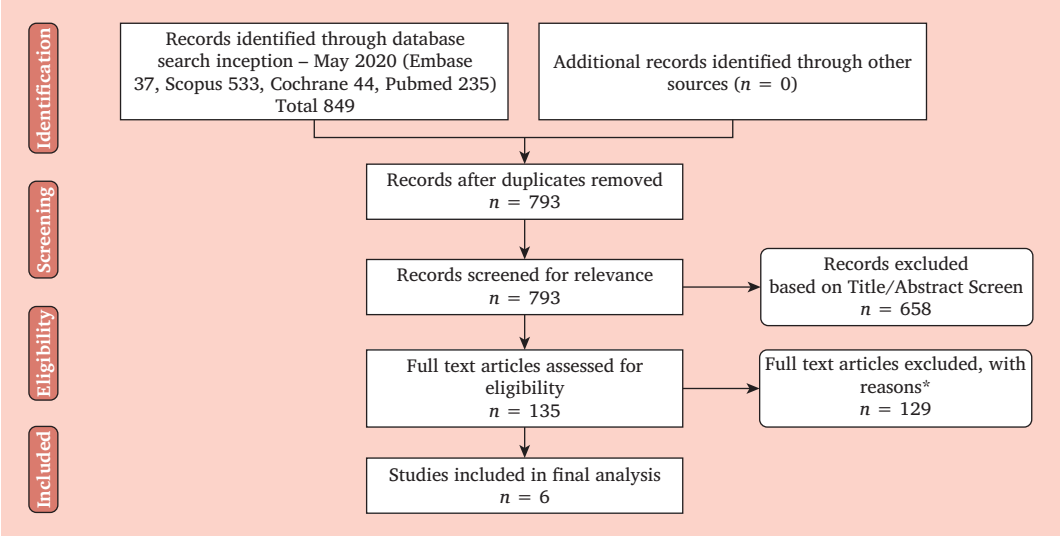

Figure 1. PRISMA flow diagram.

Table 1. Of these, 129 articles were excluded for the following reasons; study focus on critical limb ischaemia (symptom duration more than two weeks) (six), no full text available (five), insufficient data on outcomes of interest (25), review articles (five), upper limb ischaemia only (two), case reports (84), included patients with any history of

malignancy ever (two). Ultimately, six articles were included for analysis. Risk of bias and quality assessment was carried out using the NIH/NHLBI Quality Assessment Tool for Observational Cohort and Cross Sectional Studies, and rated as "Good", "Fair" or "Poor". Three studies were rated as "Good", while three were rated as "Fair".

Results of individual studies

Patient demographics and study characteristics. Six studies which included 4 689 patients, 284 with cancer, were used for data extraction. Three studies compared outcomes between cancer and non-cancer patients,[8,13,19] while three included only cancer patients.[9,10,14] Study characteristics and patient demographics are given in Table 3. All surgical interventions were aimed at revascularisation and limb salvage except for one patient included in the study by Mouhayar et al.[14] who underwent primary amputation.

Javid et al.[10] performed a prospective single centre study including 20 patients with active malignancy. The most common type of cancer was breast cancer (25%). Twelve patients (60%) had metastatic disease. Sixteen (80%) had some form of adjuvant therapy within one month prior to presentation. Four patients (20%) presented with venous thromboembolism either shortly before or after the arterial event. Four patients were managed palliatively, and four others were managed conservatively (with anticoagulation, glyceryl trinitrate patches, and analgesia). Chemical sympathectomy was performed in two cases. The remaining 12 patients underwent angiography; four of whom were managed conservatively and eight surgically; all were given anticoagulation. Five had thromboembolectomy and three underwent bypass procedures. Of the three patients who underwent bypass surgery, two failed within six weeks. The first who underwent an iliofemoral and femoropopliteal bypass had further thromboses and died within six weeks. The second had a femorofemoral crossover graft, had graft thrombosis two weeks' post-operatively and required above knee amputation but died a week later. The third who underwent a femoropopliteal bypass died six months post-operatively. Five of the six thromboembolectomies failed, four within 24 hours and one at three weeks. The remaining patient had some initial improvement but died six weeks later. Three of these patients underwent repeat thromboembolectomy, two of which also failed. One subsequently had a below knee amputation and died five months later. The other patient was treated with streptokinase which failed, and she died three weeks later. Javid et al.[10] included only cancer patients in their study and reported a 10% amputation rate (two of 20) during follow up.

Table 3. Patient demographics and study characteristics.

Characteristics	Country	Study design	No. of patients	Case *vs.* non-case	Case definition	Gender	Age mean or median (range)	Mean/ median follow up	Upper *vs.* lower limb
Javid et al.[10]	UK	Prospective	20	Cancer 20	Active malignancy	M 7, F 13	Median 63 (35—86)	Median 8 weeks	Upper 1, Lower 19
Mouhayar et al.[14]	USA	Retrospective	74	Cancer 74	Active malignancy	M 34, F 40	Median 61 (25—80)	Median 8 mo	Upper 4, Lower 70
Morris-Stiff et al.[8]	UK	Retrospective	126	Cancer 14	Native vessel occlusion only (occluded grafts were excluded), any active malignancy	M 9, F 5	Mean 71.5 (47—83)	NR	NR
				No cancer 112		M 35, F 77	Mean 72.9 (43—99)		NR
Bennet et al.[13]	USA	Retrospective	4331	Cancer 136	Advanced malignancy only*	M 77, F 59	Median 66 (57—76.5)	NR	Lower 136
				No cancer 4 195		M 2 259, F 1 936	Median 69 (58—81)		Lower 4 195
Silverberg et al.[19]	Israel	Retrospective	122	Cancer 24	Active malignancy	M 15, F 9	Mean 72 (NR)	Mean 9.8 mo	Lower 24
				No cancer 98		M 52, F 46	Mean 74 (NR)	Mean 13.4 mo	Lower 98
Tsang et al.[9]	Ireland	Retrospective	16	Cancer 16	Patients with a history of cancer (13 active, 3 diagnosed >1 y previously and not undergoing active tx)	M 10, F 6	Mean 67 (NR)	Median 62 mo	Upper 5, Lower 11

* Advanced malignancy in this study was defined as follows: cancer that: (1) had spread to one site or more sites in addition to the primary site and (2) in whom the presence of multiple metastases indicates the cancer is widespread, fulminant, or near terminal.

Bennett et al.[13] performed a retrospective study using a national database. This database included only patients who underwent an operation and therefore did not include patients who did not undergo surgery. Patients with underlying advanced malignancy presenting with ALI who underwent an operation were included. Patients were classified as having advanced malignancy if they met one or more of the following criteria: 1) evidence of disseminated cancer, 2) chemotherapy within 30 days preceding index operation, 3) radiotherapy within the 90 days preceding the index operation, 4) presence of a tumour of the central nervous system. Amputation data were not recorded as a separate outcome, but as aggregate morbidity which also included surgical site infection, venous thromboembolism, pneumonia, stroke, renal failure, cardiac arrest, myocardial infarction, major bleeding, and sepsis, among others. One hundred and thirty six patients were included; 88 of whom underwent thromboembolectomy, 26 underwent thromboendarterectomy, and 22 bypass grafting. Forty one of 136 cancer patients (30.2%) died within 30 days of presentation in the study. However, despite the study including only patients with advanced malignancy, they did not have the highest 30 day mortality rate. Bennett et al.[13] also reported 30 day mortality data for patients based on type of surgical intervention; 27 of the 88 patients who underwent thromboembolectomy died within 30 days, six of the 26 patients who underwent thromboendarterectomy died in this time period and a further eight patients of the 22 who underwent bypass operations also died within 30 days.

Silverberg et al.[19] performed a retrospective study including 24 patients with active malignancy, all of whom had Rutherford IIa or IIb acute limb ischaemia. Cancer stage was reported as the following; six patients had stage I disease, one had stage II, six had stage III, nine had stage IV, and in two patients the stage was unknown. Nineteen patients underwent active revascularisation efforts (including nine patients who underwent arterial thrombolysis and a total of 15 patients who had a thromboembolectomy, of whom five were after failed thrombolysis). Five patients were suffering from advanced metastatic disease; therefore, they were not subjected to intervention given their terminal prognosis. Silverberg et al.[19] reported the lowest rate of amputation at 4.2% with just one amputation of 24 patients who presented with ALI. Five of 24 cancer patients (20.8%) died within 30 days.

Tsang et al.[9] carried out a retrospective study looking at 16 patients with ALI and active malignancy. The patients had the following types of cancer: five urogenital tract, five lung/mediastinal, four gastrointestinal, one laryngeal, one breast. All 16 patients underwent operative management with thromboembolectomy, two of which subsequently required a bypass procedure. Tsang et al.[9] reported an overall amputation rate of 37.5% in their patients (six of 16) and reported the lowest 30 day mortality with just one death of 16 cancer patients (6.3%) presenting with ALI.

Mouhayar et al.[14] performed a retrospective study including 74 patients. The Rutherford classification for ALI was recorded for each patient as follows; Rutherford I = 13, Rutherford IIa = 30, Rutherford IIb = 29, Rutherford III = 2. Twenty one patients underwent thrombolysis; seven of whom subsequently required surgery. A total of 36 patients underwent surgical intervention; 23 thromboembolectomy, seven bypass, six combination. Five patients who underwent surgical intervention failed revascularisation, and a further two patients underwent thrombolysis which failed and all required amputation. The amputation rate was recorded as 11% during follow up (eight of 74 patients). One patient was included who underwent primary amputation for late presentation with profound ischaemia. All other patients who suffered limb loss, as described above, had failed previous revascularisation attempts. Mouhayar et al.[14] found a 30 day mortality rate of 20%, with 15 of 74 patients dying during this time.

Morris-Stiff et al.[8] undertook a retrospective study based on operative registries and therefore did not include patients managed non-operatively. There were 14 patients with underlying malignancy who presented with ALI. All 14 patients underwent thromboembolectomy, one also had a bypass procedure. Underlying malignancies were as follows: bronchial adenocarcinoma (four), transitional cell carcinoma bladder (two), lymphoma (two), oesophageal carcinoma (two), bronchial squamous cell carcinoma (one), colonic adenocarcinoma (one), pancreatic carcinoma (one), gastric adenocarcinoma (one), vulval squamous cell carcinoma (one), chronic lymphatic leukaemia (one). Morris-Stiff et al.[8] identified an amputation rate of 29% during the follow up period (4/14) and 50% 30 day mortality (7/14) in their cancer cohort.

Interventions and outcomes. Table 4 provides detail on the various interventions carried out for the treatment of ALI in each study, as well as baseline performance scores, level of ischaemia at presentation, and individual outcome data.

Pooled outcomes

Amputation. Five of six studies included amputation data, while the other study[13] only included amputation as part of aggregate morbidity data along with surgical site infection, wound dehiscence, pulmonary embolism, pneumonia, mechanical ventilation, stroke, major bleeding, sepsis, urinary tract infection, nerve injury, along with some others.

For all studies, amputation included either above or below knee amputation. No patient required an upper limb amputation.

Rates varied widely for amputation among patients with active malignancy. Across five studies, the weighted average rate of amputation throughout the various follow up periods was 15% (95% CI 5.9 — 26.9).[8–10,14,19] I^2 was found to be 60%, which demonstrates significant interstudy heterogeneity. Fig. 2 includes a forest plot for overall amputation.

Mortality. Recording of mortality data varied, with 30 day mortality being the most commonly reported among studies. Javid et al.[10] recorded overall mortality without specific 30 day mortality data. Of the 264 patients with active malignancy across five studies that included data on

Table 4. Interventions and outcomes.

Characteristics	No. of patients	Case *vs.* non-case	Rutherford classification	Performance status	Intervention	Thrombolysis	Amputation	Death
Javid et al.[10]	20	Cancer 20	NR	NR	Palliation 4, conservative endovascular 12; 8 also had surgery (5 thromboembolectomy, 3 bypass)	4,	10% at 30 d (2/20), Unchanged at 1 y	50% at 3 mo, 83% at 1 y
Mouhayar et al.[14]	74	Cancer 74	R1 13, R2a 30, R2b 29, R3 2	NR	Endovascular 21 (of which 7 then had surgery), 36 surgery*; thromboembolectomy 23, bypass 7, combination 6	21; of which 7 required surgery	11% at 30 d (8/74), unchanged at 1 y	20% at 30 d, 50% at 1 y
Morris-Stiff et al.[8]	126	Cancer 14	NR	ASA class (%) 2:3:4 - 43:36:21	Surgical patients only; 13 thromboembolectomy, 1 bypass		Total throughout follow up 29% (4/14)	50% at 30 d, 100% at 60 d
		No cancer 112		ASA class (%) 2:3:4 - 41:52:9	Surgical patients only; 102 thromboembolectomy, 10 bypass		Total throughout follow up 17% (19/112)	30% at 30 d, 35% at 60 d
Bennet et al.[13]	4331	Cancer 136	NR	ASA class 4 or >60 (44.1%)	88 thromboembolectomy, 26 thromboendarterectomy, 22 bypass		NR	30.2% at 30 d
		No cancer 4195		ASA class 4 or >1216 (29.0%)	1931 thromboembolectomy, 822 thromboendarterectomy, 1442 bypass		NR	6.9% at 30 d
Silverberg et al.[19]	122	Cancer 24	All patients Class 2a or 2b	NR	5 conservative, 15 thromboembolectomy	27.6%	Total throughout follow up 4.2% (1/24)	20.8% at 30 d, 37.5% overall
		No cancer 98			71 thromboembolectomy	37.5%	Total throughout follow up 7.1% (7/98)	16.3% at 30 d, 16.3% overall
Tsang et al.[9]	16	Cancer 16	NR	NR	16 thromboembolectomy; of which 2 had a bypass		Total throughout follow up, 37.5% (6/16)	6.3% at 30 d, 12.5% overall

* Surgery excluding amputation.

30 day mortality, rates varied widely, with weighted average of 24% (95% CI 14.7 — 34.6).[8,9,13,14,19] I^2 was 60%, which demonstrates significant interstudy heterogeneity.

Some studies recorded 60 day, three month, one year, and overall mortality, details of which can be found in Table 4.

Fig. 3 shows a forest plot for 30 day mortality rates for each study among cancer patients.

DISCUSSION

Summary of evidence

Of the five studies that included data on amputation in cancer patients presenting with ALI, the weighted rate of amputation during follow up was 15% (95% CI 5.9 — 26.9).[8–10,14,19]

Five studies included 30 day mortality rates. Of the 264 patients, rates for 30 day mortality varied widely, with a pooled rate of 24% (95% CI 14.7 — 34.6).[8,9,13,14,19] This indicates that over three quarters of the malignancy cohort will survive the 30 day post-presentation period. The evidence available suggests that there is an acceptable risk of amputation in patients with cancer. In spite of the known increased risk of thrombogenesis in patients with cancer, this does not appear, based on current evidence, to translate to higher rates of treatment failure in those presenting with ALI.

The results regarding outcomes of interest are based on pooled evidence from uncontrolled case series (level 4 evidence).

Limitations

Bias within individual studies was evaluated using the NIH/NHLBI Quality Assessment Tool for Observational Cohort and Cross Sectional Studies. While three of the studies were rated as “Good”, three were rated as “Fair” and the reasons for this are outlined below.

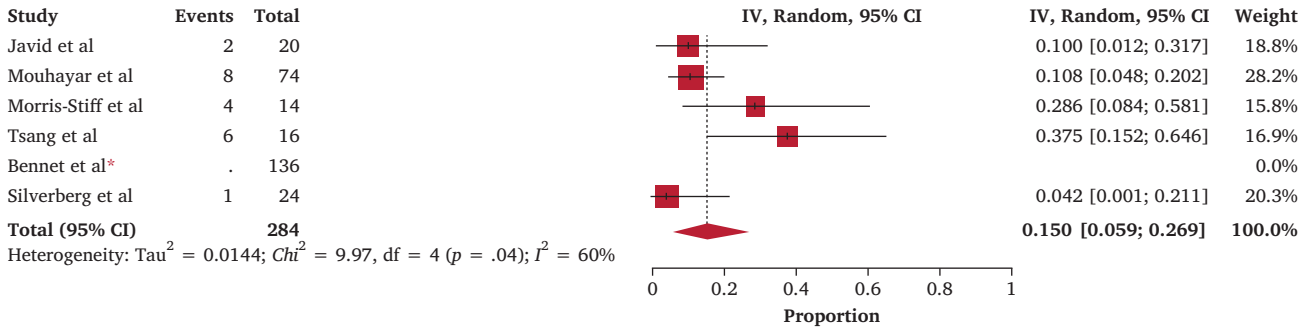

Figure 2. Forest plot demonstrating amputation proportions in cancer cohort. *The paper by Bennett et al.[13] was not included in the forest plot because it did not report on amputation outcomes.

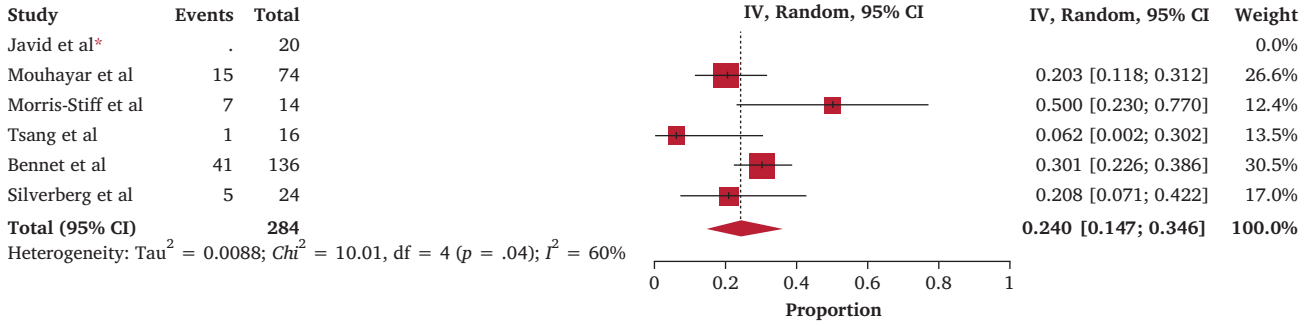

Figure 3. Forest plot demonstrating 30 day mortality proportions in cancer cohort. *The paper by Javid et al.[10] was not included in the forest plot as they did not include 30 day mortality data.

Criteria for inclusion varied among studies. Some studies included patients with advanced malignancy only.[13] Two studies pooled upper and lower limb ischaemia together in their outcome measures; however, ideally, these should be analysed separately, as there is evidence to suggest that aetiology, approach, and outcomes vary between these presentations.[20] Patients with upper limb ischaemia are less likely to require an amputation. Outcomes for different studies are heterogenous. A more nuanced approach is needed that considers baseline performance status. An important outcome predictor for limb salvage in acute limb ischaemia, in any patient, is Rutherford classification on presentation. Data were available regarding severity of ischaemia in only two of the six studies.[14,19] Furthermore, data regarding anticoagulation peri-operatively need to be recorded consistently, as this will ultimately impact on patency of revascularisation and limb salvage outcomes. Outcomes for the types of interventions in patients with cancer is important for future studies as this may highlight better or worse outcomes based on the method of revascularisation for this cohort of patients, which may be different from the general population.

Study selection processes were different among groups. Two studies used operative registries to identify retrospectively patients with ALI and cancer.[8,13] It is possible, given the inclusion of patients undergoing surgical intervention only, that substantial selection bias exists. Those with advanced disease or poor performance status may have been offered upfront palliation or amputation, which was found in some cases that included all cancer patients with ALI.[10,14] Further data on the patients not offered intervention would be interesting and it is also important to note the proportion of patients with underlying malignancy that are offered surgical revascularisation (including details about the type of intervention) *vs.* palliation and the different characteristics that determine this decision.

Conclusion

The data demonstrate that ALI outcomes for patients with cancer vary greatly across studies. Several studies have demonstrated acceptable short and medium term outcomes for patients with cancer undergoing revascularisation for acute limb ischaemia. Cancer, as a constellation of vastly differing malignancies of differing stages and undergoing a wide array of treatment modalities, should not be treated as a single entity. Future research in this area should seek to standardise inclusion criteria and case definitions in specific patient cohorts, to provide a more detailed picture of outcome measures for patients with cancer and to provide site and stage specific outcome data for the heterogenous group of malignant conditions. Evidence to date does not support upfront conservative management for patients with acute limb ischaemia and an underlying active malignancy.

CONFLICT OF INTEREST

None.

FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvsvf.2021.10.019.

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