Review article

Tumor embolism and acute arterial occlusion: A systematic review

Syed Mohammad Asim Hussain, MBChB (Hons), MRCS, MSc (Merit) *

Department of Vascular Surgery, Frimley Park Hospital, Portsmouth Rd, Frimley, Camberley GU16 7UJ, United Kingdom

Abstract

Objective: To determine common etiologies, presentations, management strategies and outcomes in patients with tumor embolism causing acute arterial occlusion.

Study design: This is a systematic review of published case reports on tumor embolism.

Search strategy: All published cases of tumor embolism in the MEDLINE and EMBASE databases were reviewed.

Inclusion and exclusion criteria: All published reports of tumor embolism were included. Studies regarding venous thromboembolism and cancer-associated thromboembolism without tumor embolization were excluded. The cases included numbered 42.

Outcome measures: These included the frequencies of different primary tumor types, clinical presentations, anatomical sites of embolization, types of intervention and outcomes including number of deaths and successful discharges.

Results: Lung cancer and Atrial Myxoma each accounted for 14 out of 42 cases (33%). There were 11 cases (26.9%) of stroke and 9 cases (21.4%) of myocardial infarction and limb ischemia. Femoral thrombo-embolectomy was performed in all 9 cases of limb ischemia and Primary coronary intervention was performed in 7 out of 9 (77.8%) cases of myocardial infarction. There were 14 inpatient deaths (33.3%) and 19 patients were successfully discharged (45.2%).

Conclusion: Lung cancer and atrial myxoma were the most common sources for tumor embolism. Acute stroke was the most common presentation. This is treated with antiplatelets or anticoagulation as well as chemotherapy and resection of primary tumor. Early revascularisation can prevent severe complications such as death, paralysis, heart failure and limb loss in selected cases of tumor embolism.

Key message: Histopathological examination of embolic tissue can demonstrate tumor tissue and alert the clinician to a cancer elsewhere. This is most likely to be lung cancer or atrial myxoma. Early revascularisation in selected cases of acute tumor embolism can prevent severe complications and these patients should not be automatically palliated due to their underlying neoplasm.

© 2022 The Author. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Keywords:
Vascular surgery
Ischaemia
Occlusion
Tumor
Revascularisation

Contents

I n t r o d u c t i o n ................................................................. 217
M a t e r i a l s a n d m e t h o d s ............................................................ 217
E t h i c a l r e v i e w .............................................................. 217
S t u d y a i m s ............................................................... 217
S t u d y d e s i g n .............................................................. 217
I n c l u s i o n a n d e x c l u s i o n c r i t e r i a ...................................................... 217
D a t a s e a r c h ............................................................... 217
S t u d y e n d p o i n t s ............................................................. 217
S t a t i s t i c a l a n a l y s i s ............................................................ 217

* Corresponding author at: 104 Climping Road, Crawley, RH11 0AY, United Kingdom.
E-mail address: mbch9sh4@doctors.org.uk (S.M.A. Hussain).

https://doi.org/10.1016/j.sopen.2022.10.006
2589-8450© 2022 The Author. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Introduction

Acute tumor embolism is a rare phenomenon with one review showing this to be a cause of arterial embolization in only 0.34% of cases [1]. Tumor embolization involves the translocation of tumor cells from a primary neoplastic source to various arterial sites resulting in occlusion and secondary complications due to ischemia. It has been known to affect blood vessels supplying the brain, heart, lung, intestine, and limbs causing the associated complications of stroke, myocardial infarction, pulmonary embolism, mesenteric infarction, and limb loss [2].

The underlying cause is generally a large and disseminated primary tumor. The risk factors for tumor embolization include type of primary malignancy, stage of tumor, tumor base size, irregular surface, and primary anatomical location [3]. Common mechanisms of embolization include tumor fragmentation resulting from direct invasion of tumor into the bloodstream or surgical manipulation [4]. The definitive diagnosis of tumor embolus is pathological with histological evidence of cancer cells seen in the embolus specimen [5]. Radiological evidence of a primary malignancy with a separate arterial occlusion may also raise suspicion of tumor embolus.

As the patient often has a poor prognosis due their underlying malignancy, it is not always clear whether surgical intervention is indicated in these cases [6]. As this is a rare condition, the evidence base is still evolving and there are no large cohort studies or guidelines available to the responsible clinician to guide management. This makes it difficult to check the appropriateness of an intervention and provide optimal patient-centred care.

Therefore, we have performed a systematic review of published case reports of arterial tumor embolism. Ultimately, this will help to facilitate a more consistent and evidence-based approach to the care of these patients. This will also help clinicians to recognize unusual presentations of malignancy.

Materials and methods

Ethical review. Ethical review is not required for this study as this is a secondary analysis of existing research literature and does not contain patient identifiable data.

Study aims. We sought to systematically review all cases of arterial tumor embolism to obtain information on tumor source, clinical presentation, management, and outcomes.

Study design. This is a systematic review of case reports on acute tumor embolism. The study has been undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines 2020.

Inclusion and exclusion criteria. All published case reports of arterial tumor embolism were included. Studies pertaining to venous thromboembolism and cancer-associated arterial thromboembolism without tumor embolization were excluded.

Data search. An electronic search was made of the MEDLINE and EMBASE medical databases in May 2021. The search terminology included the terms (Tumor Embolism) AND (Ischemia), (Occlusion) and (Infarction). This yielded 100 potential studies for review. The studies identified by the search strategy were consecutively and manually reviewed by a single reviewer. There were 42 case reports meeting the inclusion criteria.

Study endpoints. The outcome measures included the frequencies for type of primary malignancy, presence of invasion or metastases, site of embolization, surgical intervention and outcome following intervention.

Statistical analysis. Descriptive statistics have been used in this study. Data synthesis was done by manually determining frequencies from included studies.

Results

The studies included in this systematic review have been tabulated below (Table 1).

Our initial search yielded a total of 100 studies. Out of these, 42 studies met the inclusion criteria, and these were all case reports. The remaining studies were excluded as they concerned venous thromboembolism or hypercoagulability due to cancer.

Tumor source. The most common causes of tumor embolism were lung cancer and cardiac myxoma. There were 14 cases out of 42, in which the source of the tumor embolus was an underlying lung cancer. All histological types of lung cancer were prevalent including squamous cell, adenocarcinoma, small-cell, germ-cell origin, pleomorphic and mucoepidermoid types. Invariably, the cancer was of an advanced stage and demonstrated either local invasion or metastatic disease in all cases. The pulmonary vein and left atrium were the most invaded structures, with this occurring in 10 out of 14 reports.

There were also 14 cases out of 42 in which the source of tumor embolus was an underlying cardiac myxoma, which most originated from the left atrium. This is a benign tumor so does not metastasise to other structures. Since, the tumor is already present in the heart, it can easily embolize and occlude the arterial supply.

A wide variety of tumor types were implicated in the remaining cases of tumor embolus. These included 2 cases of Sarcoma and 1 case each of squamous cell esophageal carcinoma, invasive ductal breast carcinoma, prostate adenocarcinoma, signet-cell carcinoma of gastrointestinal tract origin, urothelial carcinoma. Acute myeloid leukemia, renal cell carcinoma, hepatocellular carcinoma, gastric cancer, adenocarcinoma gastro-esophageal junction, anaplastic large-cell lymphoma and myofibroblast tumor. All solid organ tumors were at an advanced stage with metastatic disease present.

Clinical presentation. The most frequent clinical presentation of tumor embolism was acute stroke resulting from occlusion of the cerebral
circulation. This occurred in 11 out of 42 cases (26.2%). The arteries affected included the distal internal carotid artery, left middle cerebral artery, right middle cerebral artery, basilar artery, and lacunar arteries.

The next most common clinical presentations were acute myocardial infarction and acute lower limb ischemia occurring in 9 out of 42 cases (21.4%), each. The most frequent site of tumor embolization was a coronary artery, occurring in 9 cases (21.4%) and leading to myocardial infarction. The arterial sites included the left anterior descending coronary artery, the right coronary artery, left circumflex artery and the obtuse marginal branch.

Acute lower limb ischemia was a common presentation, but the anatomical site of embolization and occlusion was variable. There were 5 cases of embolic occlusion at the infra-renal aorta resulting in bilateral acute lower limb ischemia. Tumor embolus of the right superficial femoral artery, left superficial femoral artery, left external iliac artery, right popliteal artery, left popliteal artery and tibial artery was also described.

Another frequent clinical presentation was pulmonary thrombotic microangiopathy and pulmonary hypertension resulting from tumor embolization to the pulmonary artery. This occurred in 7 out of 42 cases (16.7%).

The remaining cases included a wide variety of clinical presentations including renal infarcts, acute mesenteric ischemia, splenic infarcts, liver infarcts, transient ischaemic attack, and acute upper limb ischemia. In some cases, tumors embolised to multiple arterial sites simultaneously.

Management. The surgical management was informed by the clinical presentation and site of tumor embolus.

The most frequent surgical procedure performed was surgical thrombo-embolectomy with access through the femoral artery. This was used to treat acute lower limb ischemia and was performed in 9 cases, with one patient undergoing bilateral calf fasciotomies. In a couple of cases, thrombo-embolectomy was insufficient, and a vascular surgery procedure was done in addition. There was 1 case of femoral endarterectomy and patch plasty and 1 case of subclavian-bifemoral bypass.

Percutaneous coronary intervention for myocardial infarction was performed in 7 out of 9 cases. Treatment was abandoned in one case and there was insufficient data in the other case. Percutaneous thrombo-embolectomy for stroke was performed in 4 out of 11 cases. Pulmonary thrombo-embolectomy for pulmonary thrombotic angiopathy and pulmonary hypertension was performed in 2 out of 7 cases. Veno-Arterial extra-corporeal membranous oxygenation was used for cardiopulmonary support in one patient. Thrombolysis was used in 3 cases, with one case using catheter-directed thrombolysis.

There was one case of brachial embolectomy to treat acute upper limb ischemia. A laparotomy and small bowel resection were required in patient to treat acute mesenteric ischemia resulting from tumor embolism to the superior mesenteric artery.

In most patients, the underlying tumor was far too advanced to be amenable to surgical management. The only exception to this was an atrial myxoma. This was surgically excised in 10 out of 14 cases, with one case of infected left atrial myxoma also necessitating a mitral valve replacement.

Outcome. The goal of management was to prevent in-hospital death, organ infarction and limb-loss through revascularisation. There were 14 out of 42 (33%) in-hospital deaths. One patient suffered limb loss requiring an above-knee amputation. 19 patients out of 42 (45.2%) were discharged from hospital following successful revascularization and one was discharged on palliative pathway.

Discussion

This systematic review has shown that a wide variety of primary malignancies have been implicated in the phenomenon of tumor embolization. The most prevalent among these are primary lung cancers, which can invade the pulmonary veins, and atrial myxomas. These tumors can spontaneously embolize as confirmed in previous studies [50]. This is likely related to the proximity of these tumors to the heart which can pump tumor fragments into the systemic circulation resulting in wide dissemination and showering. Recent surgery is also an important risk factor for embolization as physical manipulation can cause tumor seeding and disruption and this has been corroborated in the literature [51]. All tumors were at an advanced stage demonstrating either invasion into a major blood vessel or metastatic disease, which were the primary mechanisms of neoplastic embolization. Notable rare tumors demonstrating this phenomenon included sarcoma, which infiltrated the descending aorta and internal carotid, and anaplastic large cell lymphoma, which metastasised to the heart.

In our study, the distant sites of embolization also varied widely. The most prevalent sites included the cerebral arteries and coronary arteries. This is likely related to the small size of these vessels, the proximity of these vessels to the heart, the direct pathway to these vessels and the large proportion of total cardiac output received by the cerebral and coronary vessels relative to the rest of the body.

Another frequent site of embolization were the lower limb arteries. This is related to the tendency of a large mass of tumor tissue to lodge at sites of arterial division such as the aortic bifurcation, common femoral bifurcation, and the popliteal trifurcation as the vessel caliber suddenly decreases at these points [52]. At bifurcation sites, the local blood flow is disturbed due to recirculation eddy currents, directional change and reciprocating flow patterns which are associated with low or oscillating shear stress [53]. These altered haemodynamic flow patterns can induce the activation of atherogenic and thrombogenic pathways in endothelial cells which contribute to the development of an occlusive lesion at these sites [54].

Finally, the pulmonary artery was also a frequent site of tumor embolization likely due to the frequent branches and small caliber of these vessels. In such cases, the primary malignancy was usually of gastrointestinal tract, hepatic, breast, or urological origin. These cancers can directly embolize to the pulmonary artery via the inferior vena cava, right atrium, and right ventricle. In such cases, the prognosis was poor with death occurring in 6 out of 7 patients in our study (85.7%). The specific tumors implicated in this embolization pathway included Gastric cancer, Adenocarcinoma of Gastro-esophageal junction, Hepatocellular carcinoma, Invasive ductal Breast carcinoma, Renal cell carcinoma, Urothelial carcinoma, and Adenocarcinoma of Prostate. The significance of anatomical vascular pathways to tumor embolization was particularly illustrated in a patient with a squamous cell esophageal cancer, which invaded the superior vena cava, but then embolised to the left middle cerebral artery causing a stroke, as the patient had an underlying right-to-left shunt.

It is important to differentiate the diagnosis of acute tumor embolism from the more prevalent phenomena of cancer-associated-thromboembolism as the management may differ. Tumor embolism is the physical translocation of tumor cells, cell clusters, or tumor fragments, whereas the pathophysiology of thrombo-embolism involves vessel damage, static blood flow and activation of the coagulation cascade due to the hypercoagulable state induced by cancer [55]. Tumor embolism is potentially treated with surgery or chemotherapy, while venous thrombo-embolism is treated with anti-coagulation. Clinically, the two may be indistinguishable so the diagnosis is often made on histology or post-mortem analysis [56]. The clinician should be cognisant of the fact that an acute embolism may be the first presentation of an undiscovered malignancy and investigate thoroughly. Conversely, a patient with a known malignancy may present with a tumor embolism, as opposed to a thrombo-embolism, precluding the use of thrombolysis. Tumor embolism should be part of the differential diagnosis of several medical and surgical specialties given the prevalence of neoplastic disease and the wide variety of malignancies implicated in this phenomenon.
| Article                  | Tumor type                  | Invasion or metastases | Site of embolization                                      | Management/surgical intervention                                      | Outcome                              |
|--------------------------|----------------------------|------------------------|-----------------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------|
| Cheema et al. [7]        | Non-small cell Lung cancer | Cardiac metastases     | Infra-renal aorta and bilateral common iliac arteries     | Thrombectomy                                                          | Death, Unable to be weaned            |
|                          |                            | Left atrial invasion   | Right superficial femoral artery, Superior mesenteric artery | Right femoral embolectomy and balloon angioplasty (failed)            | Morbidity. Discharged for rehabilitation unit after 3 months |
| Togo et al. [8]          | Squamous cell lung cancer  | Left atrial invasion   | Infra-renal aorta (post-op complication)                  | Thrombectomy, Left brachial artery                                     | Discharged                           |
|                          |                            | Right superficial femoral artery, Superior mesenteric artery | Bilateral femoral embolectomies (ineffective)              | Subclavian-bifemoral bypass, Brachial embolectomy                      | Death on post-operative day 5         |
| Lioudaki et al. [9]      | Left upper (LUL) Lung cancer | Invasion into left superior pulmonary vein and aortic arch adventitia | Laparotomy and small bowel resection                      | Discharged                                                             | Discharged                           |
| Cinarka et al. [10]      | LUL Squamous cell Lung cancer | Invasion into hilar structures | DSA Thrombus aortic bifurcation (post-op complication) | Discharged                                                             | Discharged                           |
| De Alcantara et al. [11] | Adenocarcinoma of right lung Adenocarcinoma of lung | Invasion into left pulmonary vein and left atrium | Left external arterial Right popliteal artery Left frontal lobe cortical infarct | Bilateral femoral embolectomy and bilateral fasciotomies               | Discharged                           |
| Schreffler et al. [12]   |                           |                        |                                                           | Bilateral embolectomy and bilateral fasciotomies                      | Discharged                           |
| Morsey et al. [13]       | Germ cell origin lung cancer |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| French et al. [14]       | Lung cancer                  |                         | Partly infiltrated descending aorta                      | Bilateral renal arteries                                               | Discharged                           |
| Tsubouchi et al. [15]    | Mediastinal Sarcoma          |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Azdaki [16]              | Left Atrial Myxoma           |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Araki, S [17]            | Squamous cell Esophageal cancer |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Liu et al. [18]          | Lung cancer                  |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Herbert et al. [19]      | Left Atrial Myxoma           |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Murugan et al. [20]      | Invasive ductal Breast cancer |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Hattori et al. [21]      | Adenocarcinoma of prostate Haematogenous metastases |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Yoshikawa et al. [22]    | Pleomorphic Lung cancer      |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Oyama et al. [23]        | Mucoepidermoid Lung cancer  |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Mouadili et al. [24]     | Left atrial Myxoma           |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Peters et al. [25]       | Infected left Atrial myxoma  |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Walong et al. [26]       | Cardiac Myxoma               |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Matthew et al. [27]      | Cardiac Myxoma               |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Gudipalli et al. [28]    | Signet cell carcinoma (GI tract origin) |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Salam et al. [29]        | Urothelial carcinoma         |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Khreis et al. [30]       | Squamous cell lung cancer Atrial myxoma |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |
| Latifi et al. [31]       |                           |                         | Bilateral renal arteries                                 | Catheter directed thrombolysis                                         | Discharged                           |

(continued on next page)
Venous control during oncological surgery was established [58]. To prevent tumor dissemination, the principle of primary tumor embolism has been well described in lung cancer cases treated with pneumonectomy [58].

Chemotherapy and radiotherapy can also increase the risk of tumor embolization through the mechanism of tumor lysis. Tumor lysis syndrome is well-described in hematological malignancies. However, the increased use of oncological cancer treatment has resulted in reports of tumor lysis syndrome in solid malignancies, which is much rarer and has a higher mortality. Recent studies in mice have shown that disseminated micro-emboli composed of debris from lysed tumor cells can cause micro-obstruction of capillary beds in various organs e.g., kidneys, lungs, brain [59]. This mechanism is further supported in a case report of endometrial cancer treated with chemotherapy resulting in pulmonary tumor embolism [60].

In our study, surgical procedures for acute tumor embolism that were commonly performed included femoral thrombo-embolectomy and primary percutaneous coronary intervention. This is related to the extensive experience of using these procedures for conventional thrombo-embolic disease. Percutaneous thrombo-embolectomy for stroke and pulmonary thrombo-embolectomy for pulmonary tumor embolism were performed less frequently as these patients were often moribund. The standard treatment for ischaemic stroke is thrombolysis using a tissue-plasminogen activator. Patients with stroke secondary to tumor embolism may not respond to this treatment as the obstructing embolus is composed of tumor tissue rather than a fibrin blood clot. In such cases, anti-platelet or anti-coagulation therapy may help address the hypercoagulability associated with cancer but the management should also include cytoreductive chemotherapy and surgical resection of the primary tumor to treat the neoplasm [61].

In cases where the primary tumor was an atrial myxoma, surgical excision was commonly performed as this is a benign and curative procedure. Limb salvage was achieved in all 3 cases, but the morbidity outweighing the risks was considerable.

Table 1 (continued)

| Article | Tumor type | Invasion or metastases | Site of embolization | Management/surgical intervention | Outcome |
|---------|------------|------------------------|----------------------|----------------------------------|---------|
| Goddard et al. [32] | Neuroendocrine lung cancer | Invasion into pulmonary vein | Artery, coronary artery Basilar artery (stroke) | Endovascular embolectomy | Death |
| Carnevale et al. [33] | Acute myeloid leukemia | | Femoral artery Tibial artery | Femoral embolectomy, common femoral endarterectomy, and patch plasty and tibial embolectomy | Discharged |
| Fukarni et al. [34] | Sarcoma | Invasion into pulmonary vein | Internal carotid artery (stroke) | Percutaneous embolectomy Thrombolysis, Angio gram | Discharged |
| Ali et al. [35] | Atrial Myxoma | | Coronary artery (Myocardial infarction) | | |
| Senyei et al. [36] | Renal cell carcinoma | Invasion into renal vein and pulmonary artery metastases | Pulmonary artery (pulmonary hypertension) | Surgical excision Pulmonary thrombo-embolectomy | Discharged |
| Whealon et al. [37] | Hepatocellular carcinoma Gastric cancer | Invasion into inferior vena cava | Bilateral pulmonary arteries | Surgical thrombo-embolectomy | Death |
| Iwashita et al. [38] | Gastric cancer | | Pulmonary artery (pulmonary thrombotic angiopathy) | Veno-arterial Extra-corporeal membrane oxygenation (ECMO) PCI and thrombectomy | Discharged |
| Waithayawongsakul et al. [39] | Atrial Myxoma | | Left circumflex (MI) | | |
| Ohshima et al. [40] | Squamous cell lung cancer | | Abdominal aorta (bilateral renal infarcts, splenic infarcts, liver infarcts and brain infarcts) | Surgical excision | Death |
| Rudkovaia et al. [41] | Adenocarcinoma Gastro-esophageal junction | Metastases | Pulmonary arteries (pulmonary hypertension) | | Death |
| Zizi et al. [42] | Cardiac Myxoma | | Infra-renal aorta | Embolectomy | Death |
| Ali et al. [43] | Cardiac Myxoma | | Right coronary artery (Acute MI) | PCI | Discharged |
| Nogai et al. [44] | Anaplastic large cell lymphoma | Cardiac metastases | Right anterior tibial, Left popliteal artery Coronary artery (MI) Right middle cerebral artery (stroke) | Surgical Excision | Discharged |
| Cannarine et al. [45] | Adenoid cystic carcinoma | | | | |
| Dimitrovie et al. [46] | Lung cancer | Invasion into left atrium | | | |
| Selby et al. [47] | Atrial myxoma | | TIA Left main coronary artery (Acute MI) | Surgical excision Percutaneous coronary intervention | Discharged |
| Khewi et al. [48] | Myofibroblast tumor | | | | |
| Pineda et al. [49] | Left atrial myxoma containing malignant | | | | |

Currently, there is little research data to decide regarding the appropriateness of surgical intervention for this condition. Both conservative management and surgical intervention may be reasonable options due to equivalent long-term outcomes as prognosis is ultimately determined by the stage of malignancy. In one small case series a brachial embolectomy was performed on two patients with upper limb arterial embolism associated with malignancy whilst a third patient was managed conservatively [62]. Limb salvage was achieved in all 3 cases, but long-term prognosis remained poor due to malignancy.

Our results show that the outcome of surgical intervention resulted in a successful discharge more often than an adverse outcome such as inpatient hospital death, organ infarction or limb loss. This is a noteworthy finding showing that the benefits of surgery outweigh the risks in selected cases of acute tumor embolism.
The limitation of this systematic review is that it is retrospective in nature, it only includes case reports due to the rarity of the condition, missing data in some case reports and lack of data collection regarding demographics, co-morbidities, and clinical, biochemical, radiological, and histological findings.

The strengths of the systematic review include a comprehensive search strategy encompassing two main databases, clear inclusion and exclusion criteria, manual identification of relevant studies without algorithm or automation, tabulation of individual studies with data, simple synthesis methods such as manual determination of frequencies and the use of simple and descriptive statistics. The risk of bias was low as all included studies were given equal weight.

Early surgical intervention can potentially prevent devastating complications such as death, disabling stroke, severe heart failure, bowel infarction and limb loss. This can greatly improve the patient's quality of life in the final stages of their malignancy. Case selection will be key as terminal disease, multiple co-morbidities, marked derangements in biochemistry and physiology, and poor baseline functioning are likely to preclude surgical intervention. In such cases, palliative management will be more appropriate.

In future, it may be beneficial to determine immediate, short, and medium-term prognostic outcomes following surgical intervention in cases of acute tumor embolism. This will help inform a consistent and appropriate management strategy.

Conclusion

This systematic review confirms that primary lung cancer and atrial myxoma are the most common sources of tumor embolism. Generally, thoracic tumors embolise to the systemic circulation via the heart and major arteries whereas abdominal tumors embolize to the pulmonary circulation via the inferior vena cava. Overall, acute ischemic stroke, resulting from embozilization to the cerebral circulation, is the most common clinical presentation. In addition to anti-platelets or anticoagulation, the treatment for this should also include cytotherapeutic chemotherapy and surgical resection of the primary tumor.

Early surgical intervention for acute tumor embolism can prevent devastating complications such as death, paralysis, heart failure, bowel resection and limb loss and enable successful discharge in selected cases. This is most often seen with femoral thromboembolus for tumor embolism of lower limb arteries and primary percutaneous coronary intervention for tumor embolism of the coronary arteries.

Ethical approval

As this is a review article, ethical approval is not required as per international standards and the policy of Frimley Health NHS Foundation Trust.

CRediT authorship contribution statement

1. Syed Mohammad Asim Hussain, was involved in the conception, design, data collection, analysis, and write-up of this manuscript. I would also like to acknowledge the contribution of the library staff at the Pennine Acute NHS Trust, who facilitated with the data search.

Funding statement

No funds were used in the production of this manuscript.

Data availability statement

The studies supporting the findings of this systematic review are available with the author and have been stated and referenced in this manuscript.

Declaration of competing interest

The author does not have any competing interests.

References

[1] Misrolov M, Lazar D, Aleksandar M, et al. Rare forms of peripheral arterial embolism. Vascular. 2005;13:222–9.
[2] Moraesch MD, Shanik GD. Tumor embolus: a case report and review of literature. Ann Vasc Surg. 2003;17:210–3.
[3] Liu Y, Wang J, Coo L, et al. Risk factors of embolism for the cardiac myxoma patients: a systematic review and meta-analysis. BMC Cardiovasc Disord. 2020;28:348.
[4] Chandler C. Malignant arterial tumor embolization. J Surg Oncol. 1993;52:197–202.
[5] He X, Anthony DC, Catoni Z, Cao W. Pulmonary tumor embolism: a retrospective study over a 30-year period. Pulm One. 2021;16(6):e2055917.
[6] Tsang JS, Naughton PA, O’Donnell J, et al. Acute limb ischemia in cancer patients: should we surgically intervene? Ann Vasc Surg. 2011;25(7):954–60.
[7] Cheema A, Karawada T, Bajwa R, et al. Tumour embolization an unusual complication of metastatic lung carcinoma. Am J Respir Crit Care Med. 2018;197:A4017.
[8] Togo S, Yamaoka T, Morita K, et al. Acute lower limb ischemia and intestinal necrosis due to arterial tumor embolism from advanced lung cancer: a case report and literature review. Surg Case Rep. 2018;4:42.
[9] Lisoudaki S, Kontopoulos N, Paliosoudakis S, et al. Acute aortic occlusion due to tumor embolism in a patient with lung malignancy. SAGE Open Med Case Rep. 2017 Jul; 18(5) [20503131X17770627].
[10] Cinarka H, Kayhan S, Gumus A, et al. A rare clinical entity of lung cancer: metastatic peripheral arterial embolism. Respir Case Rep. 2014;3(2):118–21.
[11] De Alcantara V, de Souza C, Borges R, et al. Acute arterial occlusion of lower limbs caused by tumor embolism in a patient with lung neoplasia. J Vasc Bras. Dec 2012;11(4).
[12] Schroff S, Paolo W, Kloss B. Spontaneous showering of tumor emboli in a patient with advanced primary lung cancer: a case report. Int J Emerg Med. 2012;5:27.
[13] Morsey H, Aslam M, Standfield N. Tumor embolization causing acute ischemia with sometimes fatal results. Case report and review of literature. Int Angiol. 2004 Mar;23(1):82–4.
[14] French BG, Peebles SE, Davidson KG, et al. Massive tumour embolus from primary lung cancer. Aust N Z J Surg. 1992 Apr;62(4):317–9.
[15] Tsubouchi K, Ibusuki R, Makimori K, et al. Tumor embolism as a cause of renal artery occlusion and acute kidney injury diagnosed and treated with endovascular intervention in a patient with mediastinal undifferentiated sarcoma. Intern Med. 2021 Nov; Jun 15;60(12):1907–10.
[16] Azdaki N, Maes N, Hosseinzadehmaleki et al. Failed primary percutaneous coronary intervention in a middle-aged man without cardiovascular risk factors: left atrium myxoma. Pan Afr Med J. 2020;36:6.
[17] Arakli S, Maekawa K, Kobayashi K, et al. Tumor embolism through right–left shunt due to venous invasion of esophageal carcinoma. J Stroke Cerebrovasc Dis. 2020 Dec; 29(12):105352.
[18] Liu J, Chen H, Xie X, et al. Lung tumor presenting with acute myocardial infarction and lower extremity arterial embolism. BMJ Cardiovasc Disord. 2020;20:482.
[19] Herbert C, Morgan J, Forbes K et al. Getting to the heart of the white matter. Arch Dis Child. 2020;107:132–7.
[20] Murugan L, Saha A, Mabourakh D et al. Tumoral pulmonary hypertension: a rare but deadly complication of metastatic cancer. Chest, Vo 158(4) [A2101-A2102]
[21] Hattori T, Iegami Y, Matsunaga S, et al. Microscopic pulmonary tumour embolism from adenocarcinoma of the prostate. JIB Case Rep. 2020 Jun 18;3(5):161–5.
[22] Yoshikawa S, Kamide T, Kasakura S, et al. A case of cerebral infarction due to pleomorphic carcinoma of the lung. Surg Neurol Int. 2020;11:217.
[23] Oyama T, Asai T, Miyazawa T, et al. A case of cerebral tumor embolism from extracardiac lung cancer treated by mechanical thrombectomy. NMC Case Rep J. 2020 Jun 24;7(3):101–5.
[24] Moudalil M, Tardy A, El Fatmi B, et al. 853 bilateral lower limb ischemia in a healthy young man what if the heart was hiding the etiology. Eur Heart J Cardiovasc Imaging. January 2020;21(1) [319.501].
[25] Peters MJ, Tuwariqi KW, Farah MG. A case of infected left atrial Myxoma presenting as ST-elevation myocardial infarction (STEMI). Am J Case Rep. 2019 Dec;24(20): 1385–9.
[26] Walong E, Oduor J. A 26-year-old female patient with a fatal stroke due to embolism of cardiac Myxomatous neoplasm diagnosed at a Kenyan forensic autopsy service: a case report. Forensic Sci Int Rep. July 2019;1:100013.
[27] Mathew R, Agrawal N, Aggarwal P, et al. Atrial Myxoma presenting as acute bilateral limb ischemia. J Emerg Med. 2019 Nov;57(5):710–2.
[28] Gudipally S, Gowda V, Minupuri A et al. P1792- signet ring cell carcinoma: a rare cause of pulmonary hypertension. Chest. 2019.;156(4) [Supp A554].
[29] Donnell J, et al. Acute limb ischemia with fatal right atrial myxoma embolus: a case report. Am J Cardiol. 2019;123(10):1549–50.
[30] Salmi N, Pathak K, Friedman E, et al. Pulmonary tumor thrombotic microangiopathy: a rare cause of pulmonary hypertension. Chest. 2019;156(4) [Supp A554].
[31] Khiweis M, Soliman M, Akanbi O, et al. Unusual cause of right flank pain. Chest annual meeting; 2019.
[32] Latif AN, Ibe U, Guanara J. A case report of atrial myxoma presenting with systemic embolization and myocardial infarction. Eur Heart J Case Rep. 2019 Jul 11;3(3).
[33] Goddard JK, Nussbaum ES, Madison M, et al. Endovascular aspiration to treat acute ischemic stroke caused by embolic carcinoma. Interv Neuroradiol. 2019;25(4): 403–6.
[34] Carnevale ML, Phair J, Yau P, et al. Blast cell arterial embolus in acute myelogenous leukemia. Ann Vasc Surg. 2019 Apr;56:351.e9–351.e11.

S.M.A. Hussain
Surgery Open Science 10 (2022) 216–222
[34] Fukami Y, Yanaguchi K, Miyasaka A, et al. Acute ischemic stroke due to undifferen-
tiated sarcoma: a case report and literature review. Intern Med. 2019;58(1):115–8.
[35] Ali A, Raza S, Abbas T. Acute myocardial infarction as a first presentation of left atrial
myxoma in a young patient. Eur Heart J Cardiovasc Imaging. Jan 2019;20.
[36] Senyei G, Papamatheakis D, Auger W, et al. Metastatic renal cell carcinoma mimick-
ing chronic thromboembolic pulmonary hypertension. Am J Respir Crit Care Med.
2018;197:A1704.
[37] Whealon S, Friedman E. An unusual cause of massive pulmonary embolism. Am J
Respir Crit Care Med. 2018;197:A3728.
[38] Iwashita Y, Hiramoto T, Suzuki K, et al. Possibility of venoarterial extracorporeal
membraneous oxygenator being a bridging therapy for hemodynamic deterioration of
pulmonary tumor thrombotic microangiopathy prior to initiating chemotherapy: a case report. Medicine (Baltimore). 2018 Sep;97(37):e12169.
[39] Waithayawongsakul P, Limsuwan A, Jongviriyavong P, et al. Thrombus aspiration in
acute myocardial infarction in children with intra-cardiac mass. Cardiol Young. Apr
2018;28.
[40] Ohshima K, Tsujii Y, Sakai K, et al. Massive tumor embolism in the abdominal aorta
from pulmonary squamous cell carcinoma: case report and review of the literature.
Pathol Int. 2017 Sep;67(9):467–71.
[41] Rudkovskaya AA, Lo YC, Brady V, Costa J, Fares WH. A 49-year-old man with subacute
respiratory failure and interstitial lung opacities. Am J Case Rep. 2017 Aug;18:941–4.
[42] Zizi O, Benfor B, Jiber H, et al. compliqué par une occlusion aortique aiguë (À propos
d’un cas) [Intracardiac myxoma complicated by acute aortic occlusion (case report)].
Ann Cardiol Angeiol (Paris). 2017 Apr;66(2):116–8.
[43] Ali N, Zeb S. Acute myocardial infarction in a 36-year-old man from embolized left
atrial myxoma. Rawal Med J. 2016;41(1):125–7.
[44] Nagai K, Suyama Y, Koga D, et al. Anaplastic lymphoma kinase-positive anaplastic
large cell lymphoma with cardiac metastasis and arterial tumor embolisms during
first-course chemotherapy. Case Rep Oncol. 2016;9:440–6.
[45] Cannarile P, Cresti A, Stefanelli S, et al. Infarto miocardico come prima
manifestazione di un mixoma atriale: la bomba nel cuore. Caso clinico e revisione
della letteratura [myocardial infarction as the first manifestation of an atrial myx-
oma: the bomb in the heart. Case report and literature review]. G Ital Cardiol
(Rome). 2016 Dec;17(12):1012–6.
[46] Dimitrovčić Ana, Breitenfeld Tomislav, Supanc Višnja, Roje-Bedeković Marina, Soldo
Silva Butković, Vargek-Soltér Vesna. Stroke caused by lung cancer invading the left
atrium. J Stroke Cerebrovasc Dis. 2016;25(5):e66–8.
[47] Selby A, Taha R, Sandel S. All mixed up. J Gen Intern Med. May 2016;31(2).
[48] Kheiwa A, Turner D, Schreiber T. Left main coronary artery embolization in an 11-
year-old girl due to inflammatory myofibroblastic tumor of the mitral valve. Catheter Cardiovasc Interv. 2016 Apr;87(2):533–8.
[49] Pineda AM, Mihos CG, Nascimento FO, Santana O, Lamelas J, Beohar N. Coronary
embolization from a left atrial Myxoma containing malignant lymphoma cells. Tex
Heart Inst J. 2015;42(6):565–8.
[50] Sadat U, Noor N, See TC, et al. Peripheral arterial ischemia by primary lung tumour in
vading left atrium. Lung Cancer. 2007;57:237–9.
[51] De Boer HH, Prillelevitz HW. Massive tumour embolism. Arch Chir Neerl. 1969;21:
223–34.
[52] Saric M, Kronszon I. Aortic atherosclerosis, and embolic events. Curr Cardiol Rep.
2012;14:342–9.
[53] Asakura T, Karino T. Flow patterns and spatial distribution of atherosclerotic lesions
in human coronary arteries. Circ Res. 1990;66:1045–66.
[54] Chiu JJ, Chen S. Effects of disturbed flow on vascular endothelium: pathophysiological
basis and clinical perspectives. Physiol Rev. 2011;91:327–87.
[55] Falanga A, Schieppati F, Russo L. Pathophysicsiology 1. Mechanisms of thrombosis in
cancer patients. Cancer Treat Res. 2019;179:11–36.
[56] Price LC, Seckl MJ, Dorfmüller P, Wort SJ. Tumoral pulmonary hypertension. Eur
Respir Rev. 2019;28:180065.
[57] Fares J, Fares MY, Khachfe HH, et al. Molecular principles of metastasis: a hallмарк
of cancer revisited. Sig Transduct Target Ther. 2020;5:28.
[58] Senderoff E, Kirschner PA. Massive tumor embolization during pulmonary surgery. J
Thorac Cardiovasc Surg. 1962;44:528–35.
[59] Vogel P, Fletcher JM, Liang Y. Spontaneous acute tumor lysis syndrome as a cause of
early deaths in short-term carcinogenicity studies using P53 +/− mice. Vet Pathol.
2010;47:719–24.
[60] Ito T, Otta T, Narumi M, Sakai H, Seino M, Sudo T, et al. Tumor lysis syndrome asso-
ciated with docetaxel and carboplatin in a case with recurrent endometrial cancer.
Gynecol Oncol Rep. 2018;24:21–3.
[61] Navi BB, Kastner SE, Ellkaid MSV, et al. Cancer and embolic stroke of undetermined
source. Stroke. 2021 Mar;52(3):1121–30.
[62] Harnarayan P, Islam S, Narayningsh V. Arterial embolism in malignancy: the role of
surgery. Ther Clin Risk Manag. 2021 Jun;17(7):635–40.