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REVIEW ARTICLE

Surgical and interventional radiological management of adult epistaxis: systematic review

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Abstract

Background: There is variation regarding the use of surgery and interventional radiological techniques in the management of epistaxis. This review evaluates the effectiveness of surgical artery ligation compared to direct treatments (nasal packing, cautery), and that of embolisation compared to direct treatments and surgery.

Method: A systematic review of the literature was performed using a standardised published methodology and custom database search strategy.

Results: Thirty-seven studies were identified relating to surgery, and 34 articles relating to interventional radiology. For patients with refractory epistaxis, endoscopic sphenopalatine artery ligation had the most favourable adverse effect profile and success rate compared to other forms of surgical artery ligation. Endoscopic sphenopalatine artery ligation and embolisation had similar success rates (73–100 per cent and 75–92 per cent, respectively), although embolisation was associated with more serious adverse effects (risk of stroke, 1.1–1.5 per cent). No articles directly compared the two techniques.

Conclusion: Trials comparing endoscopic sphenopalatine artery ligation to embolisation are required to better evaluate the clinical and economic effects of intervention in epistaxis.

Key words: Epistaxis; Surgical Procedures; Operative; Radiology; Interventional; Ligation

Introduction

Many cases of epistaxis arise from Little's area on the anterior nasal septum, and can be managed by direct treatments (nasal packing and cautery), whilst controlling underlying risk factors.[1] In some cases, and particularly those involving posterior site bleeding, primary direct treatment may be ineffective, and affected patients may require surgical or endovascular treatment.[2]

Whilst epistaxis may sometimes be managed by cautery performed under general anaesthesia, the focus of surgical intervention is usually the ligation of vessels supplying the nasal mucosa, performed via an open or endoscopic approach. Historically, the surgical treatment of refractory posterior epistaxis consisted of transantral surgical ligation of the internal maxillary artery, with or without ligation of the anterior ethmoidal artery. More recently, endoscopic ligation of the sphenopalatine artery has become the mainstay of surgical treatment for epistaxis in most UK hospitals. Despite this, evidence is lacking with regard to the superiority of sphenopalatine artery ligation over transantral maxillary artery ligation or embolisation. There is no standardised threshold for surgical intervention, with significant variation seen in pre-operative management.

Interventional neuroradiology is an evolving field.[3] First described for epistaxis in 1974 by Sokoloff *et al.*,[4] endovascular embolisation of the internal maxillary artery appears to represent an effective alternative to surgery. Current practice involves super-selective embolisation of distal branches of the internal maxillary artery and other extracranial collaterals, guided by angiography. This procedure is usually performed under local anaesthetic, with or without sedation, using a variety of embolisation materials. In the UK, endovascular procedures for epistaxis are only performed in selected centres.

The appropriate place for surgery and interventional radiology in the stepwise management of refractory epistaxis, and their associated risks, have not been well characterised. As a result, the UK currently has no best practice guidelines regarding the appropriate indications for these treatments in patients with epistaxis.

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Aims

This review aimed to address the following key clinical questions that were identified relating to the management of epistaxis with surgery and interventional radiology: in patients treated in hospital with refractory epistaxis, how effective is surgery compared to direct treatments (nasal packing and cautery)?; and, in patients treated in hospital with refractory epistaxis, how effective is interventional radiology compared to direct treatments and surgery?.

Materials and methods

This work forms part of a set of systematic reviews designed to summarise the literature prior to the generation of a UK national management guideline for epistaxis. This review addresses the final identified research domain: surgical management and radiological intervention. A common methodology has been used in all reviews, described in the first of the publications.[5] Studies were only included if they primarily included patients aged 16 years and above who were treated for epistaxis within a hospital environment. The search strategy for this review can be found in the online supplementary material that accompanies this issue.

All forms of endovascular embolisation were included in the current review. Surgical management was included where a named vessel was targeted, whilst endoscopic cautery of the nasal mucosa was excluded. The topics of particular interest were: efficacy of haemostasis, appropriate timing of the interventions, economic assessment, patient-reported outcomes and adverse effects. Adverse effects were defined as minor if they were transient and local. Complications associated with permanent or significant morbidity, or mortality, were defined as major.

All randomised controlled trials, controlled and uncontrolled longitudinal studies, and cross-sectional studies were accepted for analysis. Controlled surgical studies were included where the comparator was non-surgical direct management (nasal packs or cautery) or other forms of surgical ligation. Studies that compared surgical ligation to embolisation are discussed within the interventional radiology section.

Surgical intervention

Results

In the surgery review, 37 studies were included for analysis (Appendix I). Figure 1 illustrates the search and article selection process.

Only one of the included studies was a randomised controlled trial.[6] Thirteen retrospective controlled studies[7–19] and 23 retrospective uncontrolled longitudinal studies[20–42] were accepted for analysis. The number of participants in the included studies varied from 8 to 4662. No sample size calculations were performed in any of the studies. Five studies were multicentre.[18,20–22,27] Settings included hospitals within the UK, USA, Canada, France, Egypt, Iran, Italy, China, Brazil and Malaysia.

The only identified randomised controlled trial compared sphenopalatine artery ligation to packing.[6] Regarding the controlled retrospective studies, three analysed early versus delayed surgical management, three compared sphenopalatine artery ligation to other surgical options, two compared surgical ligation to nasal packing, and the final five studies compared surgery to embolisation. Although the latter studies were identified during the surgical systematic review, the results will be discussed in the embolisation section to prevent duplication.[8,9,11,16,19]

Of the uncontrolled longitudinal studies, 16 evaluated sphenopalatine artery ligation, 4 evaluated internal maxillary artery ligation, 1 investigated anterior ethmoidal artery ligation and 2 studies evaluated external carotid artery (ECA) ligation. There has been a shift towards more recent publications reporting outcomes of sphenopalatine artery ligation, reflecting a change in clinical practice.

Summary of evidence

Different surgical techniques. Results from studies relating to the surgical treatment of epistaxis are summarised in Table I.[6,7,11–13,15,17,18]

Three single-centre, retrospective controlled studies compared sphenopalatine artery ligation to other surgical methods. Srinivasan *et al.*[15] and Umapathy *et al.*[17] reported on sphenopalatine artery ligation with a variety of comparators: submucous resection, ECA ligation and isolated anterior ethmoidal artery ligation. The third study compared isolated sphenopalatine artery ligation to sphenopalatine artery ligation with the addition of anterior ethmoidal artery ligation.[7] The average follow-up period ranged from 10 to 43 months. Umapathy *et al.* reported success rates of 98 per cent for sphenopalatine artery ligation compared to 70 per cent for other surgical methods.[17] Srinivasan *et al.* reported a comparable success rate (90 per cent); however, the authors did not publish the success rate for non-sphenopalatine artery surgery.[15] Asanau *et al.* reported that the long-term success rate (more than two weeks after surgery) may be increased to 100 per cent with the concurrent use of anterior ethmoidal artery ligation, compared to a 85 per cent success rate with isolated sphenopalatine artery.[7] However, the difference between the two groups was not statistically significant and sample sizes were small ($n = 20$ and $n = 25$, respectively).

Uncontrolled longitudinal series reported comparable long-term success rates for sphenopalatine artery ligation (73–100 per cent), internal maxillary artery ligation (64–100 per cent), isolated anterior ethmoidal artery ligation (100 per cent) and ECA ligation (88–93 per cent). The average success rate across all studies was 88 per cent for sphenopalatine artery ligation and 84 per cent for internal maxillary artery ligation.

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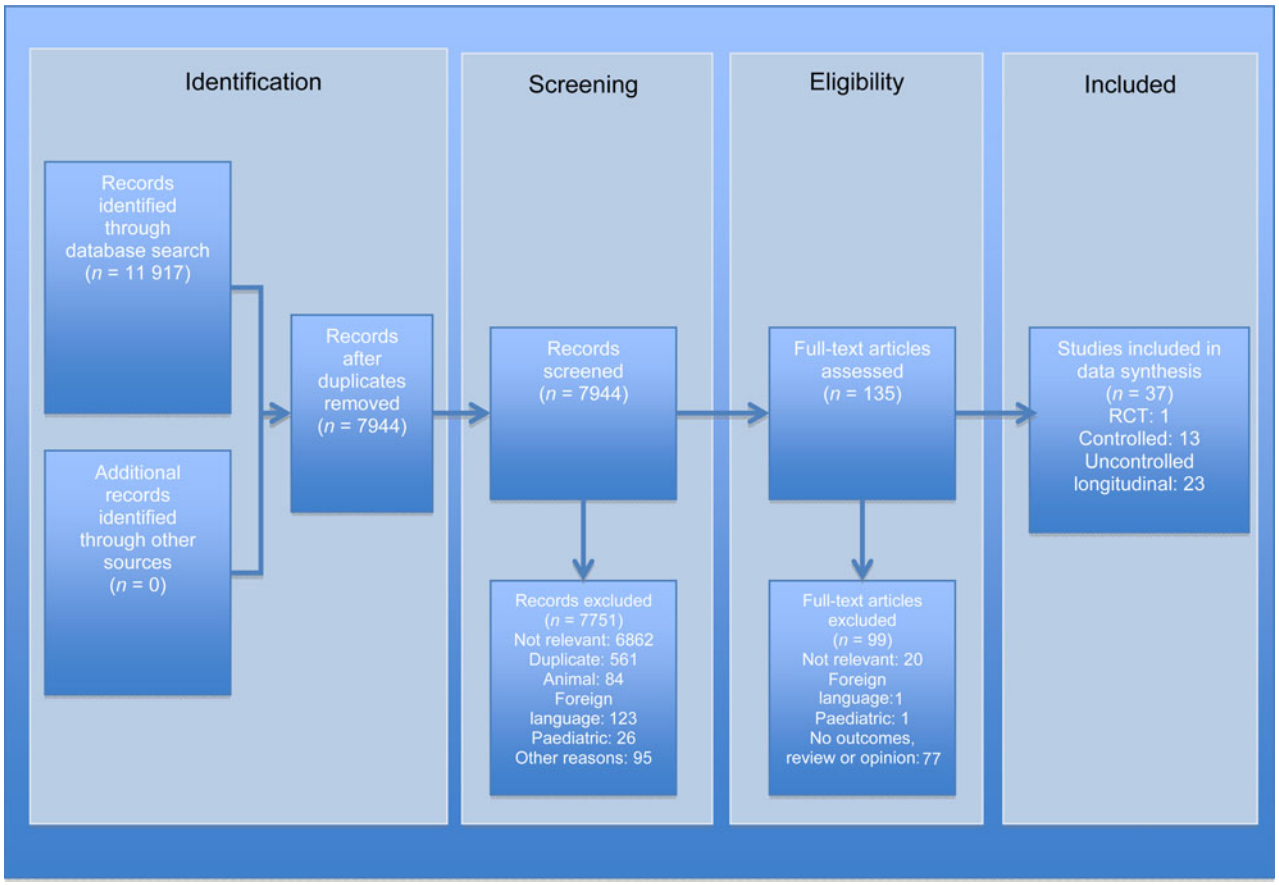

FIG. 1

Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') diagram for the surgery review, mapping the number of records identified, included and excluded during different review phases. RCT = randomised controlled trial

TABLE I

SUMMARY OF STUDIES COMPARING SURGERY TO PACKING AND OTHER TECHNIQUES

Study (year) by comparison	Groups (number of patients)	Success or 'non-recurrence' (%)	Average length of stay (days)	Cost per patient per stay (US$)
Surgery *vs* repeat packing				
– Moshaver *et al.*[6] (2004)	SPA (9)	89	1.6	5133
	Packing (10)	50	4.7	12 213
– Schaitkin *et al.*[13] (1987)	Surgical intervention (17)	88	7.2	9750
	Packing (31)	48	5.8	2744
– McDonald & Pearson[12] (1980)	IMA (46)	87	9.3	NR
	Packing (30)	50	>13	NR
SPA ligation *vs* other surgical methods under GA				
– Asanau *et al.*[7] (2009)	SPA (20)	85	5.8	NR
	SPA + AEA (25)	100	8.6	NR
– Srinivasan *et al.*[15] (2000)	SPA ± AEA (10)	90	2.1	NR
	Variety of others (8)	NR	3.9	NR
– Umapathy *et al.*[17] (2005)	SPA (41)	98	3	NR
	Variety of others (37)	70	6	NR
Surgery *vs* packing & embolisation				
– Villwock & Jones[43] (2013)	Surgery (2706)	NR	3.9	11 354
	Packing (30 389)	NR	3.2	6808
	Embolisation (1956)	NR	4.1	22 347
– Klotz *et al.*[11] (2002)	Surgery (61)	90	2.1	3851
	Packing (126)	62	5.3	5136
	Embolisation (16)	75	2.6	5697

SPA = sphenopalatine artery; IMA = internal maxillary artery; NR = not reported; GA = general anaesthesia; AEA = anterior ethmoidal artery

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Surgery versus nasal packing. Four studies compared surgery to nasal packing in posterior epistaxis, including one randomised controlled trial over follow-up periods ranging from one month to three years.[6,11–13] All studies reported higher success rates for surgical ligation compared to nasal packing (87–90 per cent *vs* 48–62 per cent). In addition, Schaitkin *et al*. reported long-term success rates of up to three years.[13] However, this dataset included patients who had already undergone surgery within the packing arm and the results were interpreted with flawed methodology. The long-term data were excluded from further analysis.

Surgical technique. A variety of procedural steps were described in detail for endoscopic sphenopalatine artery ligation; these can be subdivided into pre-operative decongestion, vessel ligation selection under general anaesthesia and post-operative nasal care. The following pertains to endoscopic sphenopalatine artery ligation.

Pre-operative nasal preparation was recognised to be important; however, there was no agreed standard. Examples included Moffett's solution, a combination of lignocaine and adrenaline (e.g. Lignospan®), and xylocaine either applied topically or via infiltration. One modification described the infiltration of local anaesthesia with adrenaline to the sphenopalatine foramen to slow vascular flow.[25]

Techniques used to perform vessel ligation include metal clips, and bipolar electrosurgery with or without monopolar electrosurgery (wattage not specified). One single-centre, retrospective study evaluated predictors of procedural failure in endoscopic sphenopalatine artery ligation over a 10-year period.[28] The use of diathermy was associated with a lower risk of early and late recurrence ($p < 0.02$ and $p < 0.007$, respectively).

Following ligation, the use of post-operative packing, topical vasoconstrictors, and topical or systemic antibiotics varied, and there was no evidence to support one over another. No studies directly analysed the use of antimicrobial prophylaxis. Most studies recommended the use of saline spray, a saline douche or Otrivine® nasal spray.

A transantral approach was described for internal maxillary artery ligation using metal clips. The two studies reporting ECA ligation performed the procedure using either local or general anaesthesia, depending on patient selection.[41,42]

Cost effectiveness. The largest contemporary study addressing the cost effectiveness of surgical treatment for epistaxis was a multicentre analysis of the American Nationwide Inpatient Sample.[43] However, it was limited to US medical centres, where costs may differ from the UK. This study analysed the management of 57 039 patients admitted to hospitals between 2008 and 2010, and compared those treated with surgical ligation, embolisation or packing. Data relating to embolisation are discussed in the 'Radiological intervention for epistaxis' section below. With respect to surgical ligation and nasal packing, length of stay data were comparable, whilst cost per patient stay was higher with surgical ligation compared to packing ($11 354 *vs* $6808). The nasal packing group did not distinguish between anterior and posterior sources of epistaxis.

Of the remaining studies, two of three reported higher financial costs associated with repeated packing compared to surgery. Klotz *et al*. demonstrated that this cost more than doubled if packing failed ($3851 surgery *vs* $5136 successful packing *vs* $9117 failed packing).[11] In contrast, the third study, published in 1987, illustrated lower financial burden in those patients treated with packing.[13] All patients initially underwent nasal packing; anterior ethmoidal artery ligation with or without internal maxillary artery ligation was used as second-line therapy in those patients for whom packing failed.

Whilst it was possible to extrapolate information regarding length of stay or requirement of blood transfusion, there is no direct evidence regarding the cost effectiveness of surgical intervention in the UK.

When should surgery be considered? Three controlled retrospective studies suggested that expedited early vessel ligation was associated with lower cost, reduced length of stay and fewer blood transfusions (Table II).[10,14,18] The timing of early surgery varied between the three studies. Two studies performed targeted surgical therapy and ligation following treatment failure after removal of the first nasal pack.[10,14] Comparatively, the most recent multicentre study performed vessel ligation within 24 hours of admission.[18]

Adverse effects. Two-thirds of studies evaluating sphenopalatine artery ligation reported on complications. Across all studies, there were no major complications. The average transient complication rates were: 5.5 per cent for local nasal symptoms (such as crusting and obstruction), 7 per cent for lacrimal gland dysfunction, 0.1 per cent for epiphora and 0.3 per cent for facial pain.

Seven of nine studies on transantral internal maxillary artery ligation reported their complications. The average complication rates were: 1.9 per cent for oro-antral fistula, 15.6 per cent for permanent cheek numbness and 0.6 per cent for permanent palatal numbness. In addition, average rates of transient complications were: 3.9 per cent for nasal symptoms, 11.7 per cent for facial swelling and 2.6 per cent for intra-oral slough.

Patient-reported outcomes. An important consideration when assessing adverse effects is the patient's perspective. Patients were more satisfied with sphenopalatine artery ligation compared to packing, and opted for internal maxillary artery ligation over packing when given the choice.[6,38] In one controlled longitudinal study, 89 per cent of patients rated sphenopalatine

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TABLE II
SUMMARY OF STUDIES COMPARING OUTCOMES FOLLOWING EARLY VERSUS LATE SURGERY

Study (year)	Groups (number of patients)	Long-term success or 'non-recurrence' (%)	Average length of stay		Cost per patient per stay	
			Days	*p*	US$	*p*
Villwock & Goyal[18] (2014)	Early (1813)	NR	3.27		28 611	
	Delayed (893)	NR	5.09	<0.001	40 449	0.095
Cumberworth *et al.*[10] (1991)	Early (20)	92	8.5		NR	
	Delayed (8)	75	15.8		NR	
Small & Maran[14] (1984)	Early (8)	NR	11.5		NR	
	Delayed (8)	NR	20.9	<0.02	NR	
	Packing (10)	NR	16.9	<0.05	NR	

NR = not reported

artery ligation as 'good' or 'very good', compared to 8 per cent for non-sphenopalatine artery surgery.[17] Patient-reported outcomes were not consistently reported in the included studies, but these data suggest that patients prefer surgical management, specifically sphenopalatine artery ligation, compared to repeat nasal packing.

Radiological intervention

Results

In the interventional radiology review, 34 studies were included for analysis (Appendix II). Figure 2 illustrates the search and article selection process.

No eligible randomised controlled trials were identified. Seven retrospective controlled studies[8,9,11,16,18,19,43] and 27 retrospective uncontrolled longitudinal studies[44–70] were included for analysis. The number of participants in the identified studies ranged from 7 to 57 039.

Summary of evidence

Embolisation versus surgery or packing. Five single-centre, retrospective controlled studies compared embolisation to surgical intervention.[8,9,11,16,19] Results from these studies are summarised in Table III. The predominant surgical method used in these studies was transantral internal maxillary artery ligation, with or without additional terminal ethmoid artery branch ligation. In Klotz and colleagues' 2002 study, only 15 per cent of patients undergoing surgical intervention underwent sphenopalatine artery ligation, demonstrating that at the turn of the century the published data still preceded the now widespread adoption of endoscopic sphenopalatine artery ligation.[11] Embolisation success rates were reported as 75–92 per cent, although the definition of success was variable. These rates were comparable to or better than those for surgical or direct measures (56–90 per cent), but with small sample sizes statistical significance was not demonstrated. Twenty-six retrospective case series reporting single-centre experience of embolisation for epistaxis were identified, with success rates (71–100 per cent) similar to those from controlled studies. The average success rate of embolisation as an epistaxis treatment was 88 per cent across all studies.

Embolisation technique. The technique used was described in detail in most studies. This invariably involved a diagnostic angiogram of the internal and external carotid arteries to look for active bleeding or potentially dangerous anastomoses between the extracranial and intracranial vessels. This was followed by micro-catheterisation of the distal internal maxillary artery, and super-selective embolisation with one or a combination of materials, including polyvinyl alcohol, Gelfoam and microcoils. Most procedures were carried out under local anaesthetic via a femoral approach. Although there were no published patient-reported outcomes of tolerance or comfort, there were no reports of significant difficulty in performing the procedure under local anaesthetic with or without sedation.

One study found an inverse relationship between the number of vessels embolised and recurrence ($p = 0.04$); however, there was a concomitant increase in complications ($p = 0.004$), including soft tissue necrosis, facial pain and, in one case, transient ischaemic attack.[52]

The published evidence cannot support one method of embolisation over another, and controlled studies comparing embolic materials or embolisation technique are lacking. However, numerous studies described a technique of targeted super-selective embolisation of the distal ipsilateral internal maxillary artery where possible, with additional embolisation of facial artery collaterals or the contralateral internal maxillary artery when necessary.

Cost effectiveness. Amongst single-centre controlled studies, there are limited data comparing embolisation with surgical costs. The same is true for length of stay, although one study demonstrated a shorter length of stay when embolisation was compared with packing (2.6 days *vs* 5.3 days; $p < 0.01$).[11] The largest multicentre study reported a comparable length of stay, but significantly higher costs per patient stay with embolisation when compared to surgery or packing ($22 347 *vs* $11 354 *vs* $6808; $p < 0.01$) (Table I).[43]

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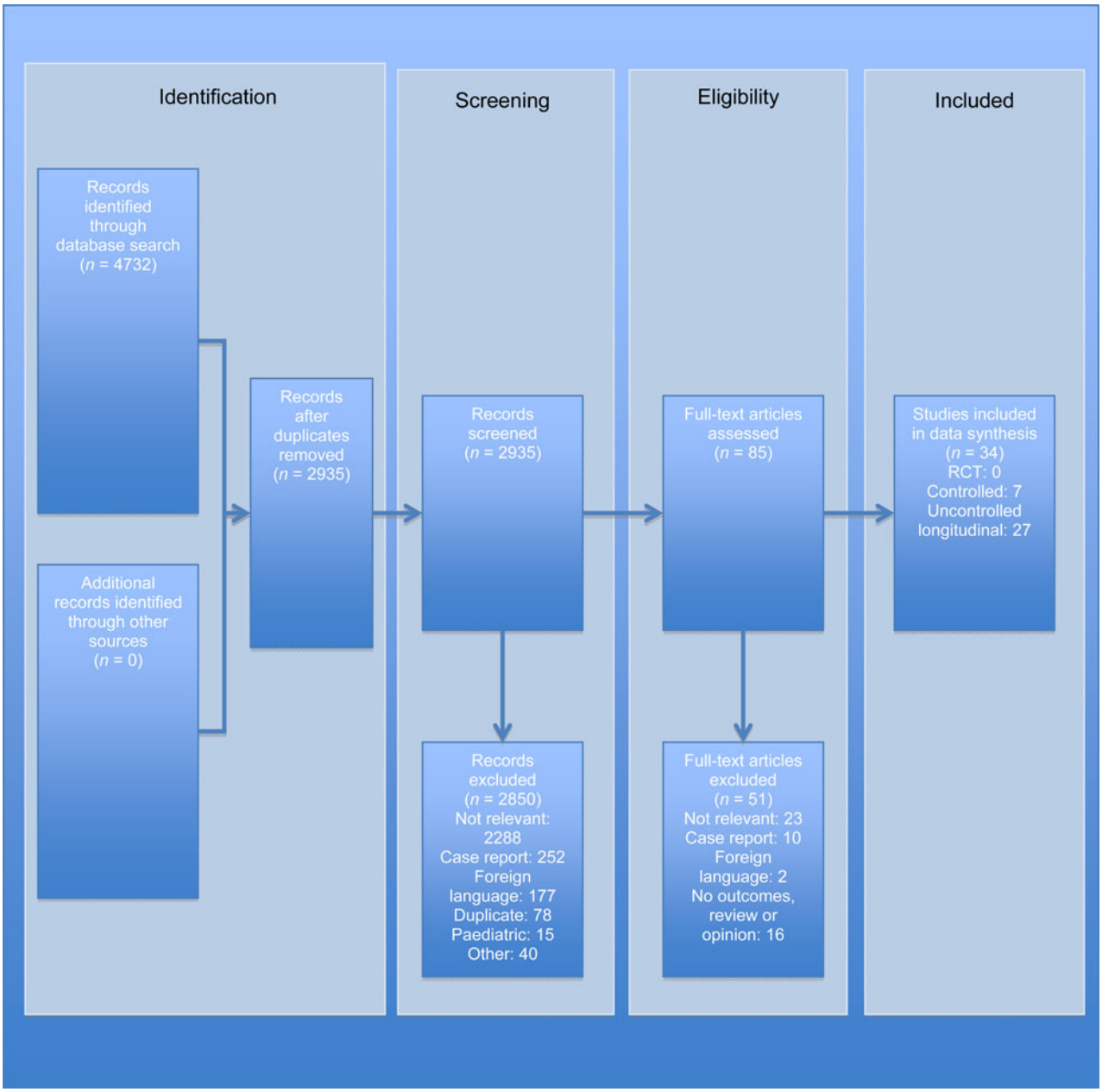

FIG. 2

Preferred Reporting Items for Systematic Reviews and Meta-Analyses ('PRISMA') diagram for the interventional radiology review, mapping the number of records identified, included and excluded during different review phases. RCT = randomised controlled trial

When should embolisation be considered? Patient selection was not directly addressed in the published literature. The majority of studies assessed the outcomes of patients with predominantly idiopathic epistaxis, who undergo embolisation after failed packing, or failed packing and failed surgical intervention. The largest controlled study excluded patients who underwent both surgical and radiological intervention, but unfortunately it did not provide data on procedure success or follow up.[43] However, it demonstrated that in the USA, embolisation is being used as a primary method to treat refractory epistaxis in large numbers, in comparison with surgical ligation (3.4 per cent *vs* 4.7 per cent of 57 039 admissions with epistaxis). Of those treated with embolisation, early intervention (within 24 hours of admission) resulted in a significantly shorter length of stay than delayed embolisation (3.0 *vs* 6.3 days; $p < 0.001$), supporting earlier intervention where possible. There was no evidence to guide clinicians on patient selection with regard to age, co-morbidity, bleeding location or bleeding severity.

Adverse effects of embolisation. There was variation in how complications are reported, particularly in the stratification of complication severity. However, across all case series, the summative rate of transient ischaemic temporofacial pain was around 10 per cent. When collating evidence from all single-centre studies, the rate of stroke was 1.1 per cent, the rate of

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TABLE III
SUMMARY OF STUDIES COMPARING EMBOLISATION TO PACKING OR SURGERY

Study (year)	Groups (number of patients)	Success or 'non-recurrence' (%)	Average length of stay (days)	Cost per patient per stay (US$)
Cullen & Tami[8] (1998)	Embolisation (28)	79	NR	4544
	Surgery (12)	73	NR	6184
della Faille *et al.*[9] (1997)	Embolisation (21)	76	4.7	NR
	Surgery (37)	65	6.5	NR
Strong *et al.*[16] (1995)	Embolisation (12)	92	2.7	6783
	Surgery (9)	56	3.9	5941
Wehrli *et al.*[19] (1988)	Embolisation (18)	78	NR	NR
	Surgery (17)	65	NR	NR

NR = not reported

tissue necrosis was 0.9 per cent and the rate of blindness was 0.3 per cent. In the only multicentre analysis, there was no significant influence of intervention modality (embolisation, surgery or packing) on the odds of mortality, but embolisation increased the odds of stroke (1.5 per cent) when compared to nasal packing (0.6 per cent) and conservative management (0.3 per cent; odds ratio = 4.660, $p = 0.003$).[43]

Limitations

There was some low- to medium-quality evidence to support surgical ligation and embolisation for refractory epistaxis. However, the number of well-designed, prospective, controlled trials assessing these interventions is limited. There was considerable heterogeneity between studies, and a resulting inability to pool results or perform meta-analysis. The key limitation in evidence is a lack of multicentre randomised trials that assessed the efficacy and safety of surgical and radiological interventions in comparison to other treatments. The majority of studies are retrospective single-centre reports, with wide variability in follow-up methodology and reporting (follow-up periods ranged from the in-patient period only to 6.7 years post-operation). Many studies only reported in-patient recurrence, leaving the potential to miss treatment failure. Conversely, those reporting recurrence of epistaxis extending several years after intervention may have limited value.

A thorough economic or cost analysis is lacking, although data from the USA do give an insight into the higher cost of embolisation as a treatment modality in comparison to surgery. It is not clear whether this holds true for other geographical areas and healthcare markets. Patient-reported disease-specific and quality-of-life outcomes were also absent in most studies.

A high risk of bias in the studies reviewed was apparent when analysed using the Cochrane Collaboration's tool for assessing risk of bias and the methodological index for non-randomised studies ('MINORS') criteria. Two of the principal outcome measures of this study, success rate and complications, were poorly defined in all of the studies, with little consistency in definition. The inter-study variation in terms of the definition and timeframe of success rate raises the question of whether this outcome was sufficiently clearly defined to be a valid outcome metric.

Conclusion

Endoscopic sphenopalatine artery ligation appears to be effective, and was associated with a favourable adverse effect profile when compared to internal maxillary artery ligation or packing. Limited evidence appears to support early surgical intervention. Most studies proposed adequate pre-operative decongestion and nasal preparation. Limited evidence suggested that use of diathermy as a method of endoscopic sphenopalatine artery ligation was associated with a lower risk of early and late recurrence rates.

Embolisation is being used as a mainstream treatment modality for refractory epistaxis in the USA within larger teaching hospitals. It is unclear whether it is being used as frequently in other countries worldwide. Success rates reported in controlled studies and case series were comparable to those for surgical intervention; however, these studies primarily performed transantral internal maxillary artery ligation, as opposed to endoscopic sphenopalatine artery ligation. Benefits of embolisation included the ability to capture diagnostic angiographic information regarding the site of bleeding, and an accurate, targeted approach to vessel occlusion. Embolisation is usually performed via a femoral approach under local anaesthetic, with or without sedation. It does require compliance with positioning. Although endoscopic sphenopalatine artery ligation can be performed under local anaesthetic, it is not done widely; radiological intervention may provide an option for those who have an absolute or relative contraindication to general anaesthetic.

Ischaemic pain and tissue necrosis are widely reported following embolisation. It could be argued that embolisation is the most appropriate option where an initial surgical intervention has failed. However, when using embolisation as a salvage procedure after failed sphenopalatine artery ligation, the source of continued bleeding is more likely to be in the territory of the ethmoidal arteries, which, being

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indirect branches of the intracranial circulation, give an inherent risk of retrograde embolisation and stroke.

There is evidence to suggest that, for patients with refractory epistaxis, surgical artery ligation and embolisation are beneficial in reducing recurrence rates. Endoscopic sphenopalatine artery ligation has a better adverse effect profile and success rate compared to other forms of surgical management. However, there were no well-designed trials comparing endoscopic sphenopalatine artery ligation with embolisation. The available evidence, in the form of uncontrolled trials, indicated that success rates were similar. The more restricted availability of interventional radiology and the costs associated with embolisation may make it less desirable in routine cases, particularly when the risk of stroke of 1.1–1.5 per cent is considered.

Adequately powered randomised controlled trials that compare endoscopic sphenopalatine artery ligation with embolisation are needed to further assess the management of refractory epistaxis. Future research should prioritise the long-term multicentre comparison of surgery and embolisation, with emphasis placed on patient-reported outcomes. Adequately powered studies that detect the clinical and economic effects of early intervention are required.

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Miss C Swords takes responsibility for the integrity of the content of the paper
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APPENDIX I
SUMMARY OF STUDIES INCLUDED IN SURGICAL INTERVENTION REVIEW

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
RCT						
Moshaver *et al.*[6] (2004)	– Single centre, in Canada – Randomised at time of initial contact – Post-discharge telephone questionnaire	– Inclusion: refractory epistaxis – Study: $n = 9$, age 57.3 years (range, 41–77 years), 4M:5F – Comparator: $n = 10$, age 66.2 years (range, 48–89 years), 7M:3F	– Study: endoscopic SPA ligation – Comparator: nasal packing	– Recurrence within 14 months – Cost – Length of stay – Patient satisfaction	– Recurrence: study = 11%, comparator = 50% ($p = 0.141$) – Cost: study = $5133.25, comparator = $12 213.19 – Length of stay: study = 1.6 days, comparator = 4.7 days ($p = 0.001$) – Patient satisfaction: study = very satisfied – 100%, comparator = painful, unpleasant – 100%	Cochrane Risk of Bias – Random sequence generation: high risk – Allocation concealment: unclear risk – Blinding of participants & personnel: unclear risk – Blinding of outcome assessment: unclear risk – Incomplete outcome data: unclear risk – Selective reporting: unclear risk – Other: low risk – No information regarding randomisation – Unable to blind because of post-surgical changes – High non-response rate for follow up (32%) – Selective reporting of satisfaction data that does not match questionnaire
Non-RCTs with comparators						
Asanau *et al.*[7] (2009)	– Retrospective study – Single centre, in France – 2-year data collection period	– Inclusion: refractory epistaxis – Study: $n = 25$, age 70.2 years, 7.3M:1F – Comparator: $n = 20$, age 72.7 years, 1M:1F	– Study: bilateral endoscopic SPA + external AEA – Comparator: bilateral endoscopic SPA	– Recurrence within 2 weeks – Recurrence after 2 weeks – Length of stay – Complications	– Recurrence within 2 weeks: study = 8%, comparator = 10% – Recurrence after 2 weeks: study = 0%, comparator = 15% – Length of stay: study = 5.5 ± 3.3 days, comparator = 3.1 ± 1.7 days – No significant complications. In both groups, 'Some patients' experienced temporary lacrimal gland dysfunction & nasal crusting	MINORS; max grade of 24 Grade: 14 – Clearly defined outcome measures – Consecutive patients – Unclear length of follow up
Cullen & Tami (1998)	See Appendix II					
della Faille *et al.*[9] (1997)	See Appendix II					

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Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Cumberworth *et al.*[10] (1991)	– Retrospective study – Single centre, in UK – 2-year data collection period	– Inclusion: epistaxis requiring packing – Study: $n = 12$, age 64.1 years – Comparator: $n = 8$, age 64.6 years	– Study: early surgical management – Comparator: delayed surgical management	– Recurrence – Cost – Length of stay – Blood transfusion	– Recurrence: study = 8.3%, comparator group = 25% – Cost: study = £850, comparator = £1580 – Length of stay: study = 8.5 days, comparator = 15.8 days – Blood transfusion: study = 3.08 units, comparator = 9.75 units	Grade: 11 – 2 variables differed in each group: timing of surgery & surgical approach (SMR *vs* ligation) – Small groups – Follow up not specified – Recurrence data not clear
Klotz *et al.*[11] (2002)	See Appendix II					
McDonald & Pearson[12] (1980)	– Retrospective study – Single centre, in USA – 8-year data collection period	– Inclusion: severe idiopathic epistaxis – Study: $n = 46$, age 53 years, 25M:21F – Comparator: $n = 30$, age 53 years, 20M:10F	– Study: IMA ligation – Comparator: nasal packing & cautery	– Recurrence within 3–5 years – Complications	– Recurrence: study = 13%, comparator = not recorded – Complications: study = infra-orbital numbness 50%, transient facial swelling 24%; comparator = sinusitis 3.3%	Grade: 8 – Groups not contemporaneous – Recurrence data not specified in control group
Schaitkin *et al.*[13] (1987)	– Retrospective study – Single centre, in USA – 4-year data collection period	– Inclusion: epistaxis – Study: $n = 17$, age 54 years (range, 32–72 years), 5M:3.5F – Comparator: $n = 30$, age 51 years (range, 24–88 years), 2M:1F	– Study: surgical therapy AEA/PEA ($n = 15$), transantral IMA ($n = 13$), septoplasty ($n = 3$) – Comparator: nasal packing & cautery	– Recurrence within 25 months – Complications – Cost – Length of stay	– Recurrence: study = 12%, comparator = 52% – Complications: study = oroantral fistulae 13%, temporary infra-orbital numbness 7%, intra-oral slough 20%; comparator = local nasal 7%, periorbital cellulitis 7% – Cost: study = $9750, comparator = $2744 – Length of stay: study = 7.2 days, comparator = 5.8 days	Grade: 16 – Flawed collection of long-term data; therefore, this set was excluded – Overlap between packing & surgical group (i.e. failed packing) moved to surgical arm
Small & Maran[14] (1984)	– Retrospective study – Single centre, in UK – 14-month data collection period	– Inclusion: refractory epistaxis – Study 1: $n = 8$, age 47 years (range, 26–69 years), 5M:3F – Study 2: $n = 8$, age 54 years (range, 22–73 years), 5M:3F – Comparator: $n = 10$, age 48 years (range, 15–78 years), 7M:3F	– Study 1: expedited early ligation following 1st pack removal. Vessel determined by operative findings: AEA ($n = 2$), IMA ($n = 6$) – Study 2: repeated packing under LA & GA before eventual ligation after failure of packing: AEA ($n = 4$), IMA ($n = 4$) – Comparator: post-nasal packing under GA but did not require arterial ligation	– Length of stay – Complications	Length of stay: study 1 = 11.5 days, study 2 = 20.875 days, comparator = 16.9 days – Complications: study 1 = adhesions 12%, oroantral fistula 12%, infra-orbital numbness 25%; study 2 = adhesions 12%, oral slough or candidiasis 12%	Grade: 10 – Low value statistical analysis – Groups not contemporaneous – Small numbers

Srinivasan *et al.*[15] (2000)	– Retrospective study – Single centre, in UK – 1-year data collection period	– Inclusion: refractory epistaxis – Study: $n = 10$, age 62.4 years (range, 47–76 years), 6M:4F – Comparator: $n = 8$ – Demographics not specified	– Study: SPA ligation – Comparator: other GA surgical procedures: AP packing + cautery ($n = 4$), AP packing + septoplasty ($n = 2$), packing + ECA ligation ($n = 2$)	– Recurrence within 10 months – Length of stay – Complications	– Recurrence: study = 10% – Length of stay: study = 2.1 days (range, 1–3 days), comparator = 3.9 days (range, 3–6 days) – Complications: both groups = 0	Grade: 8 – Non-contemporary groups – Outcome measures of comparator group do not match those of study group
Strong *et al.*[16] (1995)	See Appendix II					
Umapathy *et al.*[17] (2005)	– Retrospective study – Single centre, in UK – 7-year data collection period	– Inclusion: refractory epistaxis (total $n = 78$) – Study: $n = 41$, age 61 years (range, 22–92 years), 1.4M:1F – Comparator: $n = 37$, age 54 years (28–83 years), 1.7M:1F	– Study: SPA ligation – Comparator: non-SPA endoscopic surgery: SMR ($n = 15$), bipolar diathermy ($n = 13$), ECA ligation ($n = 2$), AEA ligation ($n = 2$), ECA + AEA ligation ($n = 5$)	– Recurrence within 43 months – Length of stay – Patient satisfaction	– Recurrence: study = 0%, comparator = 29% – Length of stay: study = 3, comparator = 6 – Patient satisfaction: study = very good or good 89%, comparator = very good or good 8%	Grade: 14 – No statistical analysis of outcomes – Telephone questionnaire not validated – 72% response rate for patient satisfaction
Villwock & Goyal[18] (2014)	– Retrospective study – US national database (20% sample of US hospitals) – 3-year data collection period	– Inclusion: all cases of epistaxis – Study 1: $n = 1813$, age 63.3 years, 53.2M:46.8F – Study 2: $n = 893$, age 64.1 years, 1M:1F – Comparator 1: $n = 1295$, age 62.8 years, 3M:1F – Comparator 2: $n = 661$, age 62.2 years, 6M:4F	– Study: surgical ligation: any of IMA, AEA, PEA, SPA, ECA. Study 1 = early, study 2 = late – Comparator: embolisation: any head & neck vessel. Comparator 1 = early, comparator 2 = late	– Length of stay – Cost	– Length of stay: study 1 = 3.27, study 2 = 5.09 ($p < 0.001$); comparator 1 = 2.97, comparator 2 = 6.27 ($p < 0.001$) – Cost: study 1 = \$28 611, study 2 = \$40 449 ($p < 0.001$); comparator 1 = \$58 697, comparator 2 = \$79 402 ($p < 0.001$)	Grade: 17 – Large national study – Same data set as Villwock & Jones[43] (2013) – Multivariate analysis – Includes reporting of further outcome data such as morbidity – No follow up once patient discharged
Wehrli *et al.*[19] (1988)	See Appendix II					
Non-RCTs without comparators						MINORS; max grade of 16
– SPA ligation						
Abdelkader *et al.*[20] (2007)	– Prospective study – Multi-centred, in UK – 3-year data collection period	– Inclusion: refractory epistaxis – $n = 43$, age 68.5 years (range, 37–85 years), 30M:13F	Endoscopic SPA ligation	– Immediate recurrence (<24 hours) – Late recurrence (>24 hours) – Length of stay (post-op)	– Immediate recurrence: 0% – Late recurrence: 9.3% – Length of stay: 1.5 days (1–4 days)	Grade: 13 – Prospective collection – Complications are not reported

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Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Eladl *et al.*[23] (2011)	– Prospective study – Single centre, in Egypt – 17-month data collection period	– Inclusion: refractory epistaxis – $n = 42$, age 51.1 years (range, 18–69 years), 23M:19F	Endoscopic SPA ligation + septoplasty when required for access ($n = 13$)	– Recurrence within 12 weeks – Objective eye dryness (Schirmer's) – Subjective nasal dryness (graded as none, mild, moderate or severe)	– Recurrence: 0% – Eye dryness 0% – Nasal dryness: none 19%, mild 48%, moderate 24%, severe 10%	Grade: 12 – Patient & clinician outcomes evaluating complications – Short follow up
Gandomi *et al.*[21] (2013)	– Prospective study – Multi-centred, in Iran – 10-month data collection period	– Inclusion: refractory epistaxis – $n = 27$, age 45.3 years (range, 17–78 years), 15M:12F	Endoscopic SPA ligation	– Immediate recurrence (<24 hours) – Early recurrence (24 hours to 2 weeks) – Late recurrence (>2 weeks)	– Immediate recurrence: 0% – Early recurrence: 11% – Late recurrence: 3.7%	Grade: 11 – Small sample size – Only 1 outcome measure – No complication reporting
Gede *et al.*[22] (2013)	– Retrospective study – Multi-centred, in Denmark – 6-year data collection period	– Inclusion: refractory epistaxis – $n = 78$, age 61.2 years (range, 14–86 years), 50M:28F	Endoscopic SPA ligation	– Recurrence within 6.7 years – Complications	– Recurrence: 22% – Complications: minor 32%	Grade: 7 – All long-term follow up by phone or mail – Poorly collated complication data – Significant loss to follow up due to mortality; therefore, potentially large number of missed complications
George *et al.*[24] (2012)	– Retrospective study – Single centre, in UK – 4-year data collection period	– Inclusion: refractory epistaxis – $n = 25$, age 64 years (range, 27–84 years)	Endoscopic SPA ligation ± AEA ligation	Recurrence within 28 months of: SPA ligation & combined surgical approaches	– Recurrence after: SPA ligation = 10.5%, combined surgery = 12%	Grade: 9 – Minimum follow-up time not stated – Gender not recorded – Telephone follow up with GP not robust & subject to bias
Harvinder *et al.*[25] (2008)	– Retrospective study – Single centre, in Malaysia – 15-month data collection period	– Inclusion: refractory epistaxis – $n = 8$, age 52.8 years (range, 26–73 years), 5M:3F	Endoscopic SPA ligation	– Recurrence within 25 months – Complications	– Recurrence: 0% – Complications: 0%	Grade: 11 – Homogeneous groups, same surgical treatment – No patients lost to follow up – Very small cohort

Howe *et al.*[26] (2012)	– Retrospective study – Single centre, in UK – 5-year data collection period	– Inclusion: refractory epistaxis – $n = 33$, age 58.4 years, 5M:28F	Endoscopic SPA ligation	– Recurrence within 5 years (max) – Length of stay – Complications	– Recurrence: 12% – Length of stay: 2 days (range, 1–22 days) – Complications: nasal dryness or crusting 28%	Grade: 6 – Vague outcomes – Significant loss to follow up – Little information regarding surgical technique
Minni *et al.*[27] (2010)	– Retrospective study – Multi-centred, in Italy – 2-year data collection period	– Inclusion: refractory epistaxis – $n = 48$, age 58.7 years (range, 26–77 years), 10M:1F	Surgical ligation of SPA (42/48, 87.5%) or AEA (6/48, 12.5%)	– Recurrence within 1 month – Complications	– Recurrence: 6.2% – Complications: nasal eschar 8.3%, craniofacial pain 2.1%, acute rhinitis 6.2%, acute sinusitis 10.4%	Grade: 8 – Good range of follow up & complications included – Mean follow up & loss to follow up not recorded – Heterogeneous group as AEA combined with SPA ligation
Nouraei *et al.*[28] (2007)	– Retrospective study – Single centre, in UK – 10-year data collection period – Binary logistic regression, log-rank statistics with Cox regression	– Inclusion: refractory epistaxis – $n = 67$, age 56 years (range, 18–89 years), 43M:24F	Endoscopic SPA ligation	– Early recurrence (2 weeks), $n/67$ (%) – Late recurrence (>2 weeks), $n/59$ (%) – Complications – Early & late predictors of failure of procedure	– Early recurrence: 12% – Late recurrence: 15% – Complications: intranasal adhesions 4.5%, septal perforation 6% – Early failure predictors: warfarin ($p < 0.03$, RR = 1.5, 95% CI = 0.9–2.6). Not using diathermy ($p < 0.02$, RR = 0.4, 95% CI = 0.29–0.54) – Early failure predictors: low platelet count on admission (Spearman's coefficient of correlation = −0.3). Not using diathermy ($p < 0.007$, 95% CI = 1.7–24.9)	Grade: 12 – Appropriate statistical analysis – Relatively large case series of similarly treated patients – Appropriate & well-defined outcome measures – Loss to long-term follow up is >5%
O'Flynn & Shadaba[29] (2000)	– Retrospective study – Single centre, in UK – Data collection period not specified	– Inclusion: refractory epistaxis within 24 hours – $n = 12$, age 65 years (range, 38–79 years), 7M:5F	Endoscopic SPA ligation	– Recurrence within 9 months – Complications	– Recurrence: 16.7% – Complications: 0%	Grade: 10 – Vague aims, & limited & poorly defined outcome measures – More descriptive than quantitative in nature – No indication if any patients were lost to follow up – Small series
Rockey & Anand[30] (2002)	– Retrospective study – Single centre, in UK – 2-year data collection period	– Inclusion: all cases of SPA ligation – $n = 10$, age 66.7 years (range, 53–79 years), 4M:6F	Endoscopic SPA ligation	– Recurrence within 6 weeks – Length of stay (post-op)	– Recurrence: 30% (diathermy 10%, clip 20%) – Length of stay: 3.3 days (1–10 days)	Grade: 11 – Small sample size – Short follow-up period

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Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Sharp *et al.*[33] (1997)	– Retrospective study – Single centre, in UK – 26-month data collection period	– Inclusion: refractory epistaxis – *n* = 10, age 53.5 years (range, 17–79 years)	Endoscopic SPA ligation	– Recurrence within 9 months – Complications	– Recurrence: 0% – Complications: 0%	Grade: 11 – Small sample size – Focus on operative technique
Snyderman *et al.*[35] (1997)	– Retrospective study – Single centre, in USA – Data collection period not specified	– Inclusion: refractory epistaxis – *n* = 15, age 49–80 years, 8M:7F	Endoscopic SPA ligation	– Recurrence within 2 months – Complications	– Recurrence: 13.3% – Complications: 0%	Grade: 8 – Small sample size – Narrative report of cases by primary surgeon – Short follow up
Tsai & Shu[34] (2002)	– Single centre, in China – Study type & data collection period not specified	– Inclusion: refractory epistaxis – *n* = 9, age 62 years (range, 38–85 years), 7M:2F	Endoscopic SPA ligation	– Recurrence within 10 months – Complications	– Recurrence: 11% – Complications: 0%	Grade: 11 – Small sample size – Few outcome measures
Wiorowski *et al.*[31] (2004)	– Retrospective study – Single centre, in France – 2-year data collection period	– Inclusion: all SPA ligation cases – *n* = 10, age 66.4 years (range, 49–88 years), 4M:6F	Endoscopic SPA ligation	– Recurrence within 1 month – Length of stay – Complications	– Recurrence: 10% – Length of stay: 2.1 days – Complications: 0%	Grade: 7 – Follow-up period not clear
Wormald *et al.*[32] (2000)	– Retrospective study – Single centre, in China – 2-year data collection period	– Inclusion: refractory epistaxis – *n* = 13, age 55.9 years (range, 23–79 years), 7M:6F	Endoscopic SPA ligation	– Recurrence within 13 months – Complications	– Recurrence: 7.7% – Complications: 0%	Grade: 9 – Small sample size – Minimal detail regarding outcome measures
Ellis & LeLiever[36] (1980)	– Retrospective study – Single centre, in Canada – 3-year data collection period	– Inclusion: refractory epistaxis – *n* = 13, age 54.7 years (range, 24–85 years)	– IMA ligation Transantral ligation of IMA	– Recurrence within 17 months – Complications	– Recurrence: 23% – Complications: 8% facial or orbital swelling, 8% mucosal bleeding or slough	Grade: 6 – Follow-up period unclear – Small cohort – Focus on operative technique

Metson & Lane[37] (1988)	– Retrospective study – Single centre, in USA – 9-year data collection period	– Inclusion: all IMA ligation cases – *n* = 100, 62M:38F – Average age reported according to outcome: recurrence 49.7 years, success 60.1 years	Transantral ligation of IMA	Recurrence within 5 years	15%	Grade: 7 – Follow-up information is unclear – Author bias
Nair[38] (1982)	– Retrospective study – Single centre, in USA – Data collection period not specified	– Inclusion: refractory epistaxis – *n* = 12, age 64 years (range, 26–90 years), gender not recorded	Transantral ligation of IMA	– Recurrence – Complications	– Recurrence: 8.3% – Complications: temporary cheek anaesthesia 25%, temporary dental anaesthesia 8.3%	Grade: 3 – Follow-up period not recorded – Pertains mainly to operative procedure
Premachandra & Sergeant[39] (1993)	– Retrospective study – Single centre, in UK – 9-year data collection period	– Inclusion: refractory epistaxis – *n* = 23, age 65 years (range, 28–85 years), 10M:13F	Transantral ligation of IMA	– Recurrence within 3.8 years – Complications	– Recurrence: 0% – Complications: temporary facial swelling + ecchymoses 26%, post-nasal drip 9%, infra-orbital nerve paraesthesia 26%	Grade: 6 Small cohort
– Other arterial ligation						
Felippu *et al.*[40] (2011)	– Retrospective study – Single centre, in Brazil – 20-year data collection period	– Inclusion: refractory epistaxis – *n* = 300, age 52 years (range, 28–80 years), 178M:122F	AEA ligation	– Recurrence within 6 months – Complications	– Recurrence: 0% – Complications: temporary nasal crusting 9%	Grade: 4 Follow up not reported
Rulon[41] (1968)	– Retrospective study – Single centre, in USA – 6-year data collection period	– Inclusion: severe posterior epistaxis – *n* = 25, age 27–80 years, 18M:7F	ECA ligation	– Recurrence between 13 months & 7 years – Complications	– Recurrence: 12% – Complications: hepatic encephalopathy 4%	Grade: 8 – Limited outcomes reported – Focused on operative technique
Waldron & Stafford[42] (1992)	– Retrospective study – Single centre, in UK – 10-year data collection period	– Inclusion: refractory epistaxis – *n* = 15, age 58.1 years (range, 30–75 years), 10M:5F	ECA ligation	– Recurrence – Length of stay – Complications	– Recurrence: 7% – Length of stay: 8 days (4–30 days) – Complications: stroke 7%	Grade: 4 – No data regarding follow-up time – Post-op care not recorded

RCT = randomised controlled trial; M = male; F = female; SPA = sphenopalatine artery; MINORS = methodological index for non-randomised studies; AEA = anterior ethmoidal artery; SMR = submucosal resection; IMA = internal maxillary artery; PEA = posterior ethmoidal artery; LA = local anaesthesia; GA = general anaesthesia; AP = anteroposterior; ECA = external carotid artery; post-op = post-operative; GP = general practitioner; RR = risk ratio; CI = confidence interval

APPENDIX II
SUMMARY OF STUDIES INCLUDED IN RADIOLOGICAL INTERVENTION REVIEW

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Non-RCTs with comparators						MINORS; max grade of 24
Cullen & Tami[8] (1998)	– Retrospective study – Single centre, in USA – 7-year data collection period	– Inclusion: refractory epistaxis – Study: $n = 28$, age 55.7 years (range, 20–96 years), 17M:11 F – Comparator: $n = 11$, age 55.5 years (range, 30–78 years), 9M:2F	– Study: embolisation – Comparator: IMA ligation ± AEA ligation	– Recurrence within 6 months – Cost – Complications	– Recurrence: study = 21%, comparator = 27% – Cost: study = $4544.85, comparator = $6184.55 – Complications: study = transient hypotension (1), groin haematoma (2), ICA intimal injury (1), MI (1); comparator = post-op sinusitis (2)	Grade: 11 – Small retrospective analysis
della Faille *et al.*[9] (1997)	– Retrospective study – Single centre, in Belgium – 9-year data collection period	– Inclusion: refractory epistaxis – Study: $n = 21$, age 55 years (range, 6–84 years) – Comparator: $n = 37$, age 59.5 years (range, 21–84 years)	– Study: embolisation – Comparator: IMA ligation ± AEA ligation	– Recurrence – Post-op length of stay – Complications	– Recurrence: study = 23.8%, comparator = 35.1% – Post-op length of stay: study = 4.7 days, comparator = 6.5 days – Complications: study = tissue necrosis (2); comparator = paraesthesia (2), infection (1), oro-antral fistula (2), nasolacrimal duct stenosis (1)	Grade: 11 – Small retrospective analysis – Non-contemporaneous groups – Lack of defined follow up
Klotz *et al.*[11] (2002)	– Retrospective study – 3 centres, in USA – 5-year data collection period	– Inclusion: refractory posterior epistaxis – Exclusions: post-surgical, trauma, HHT, coagulopathy – Study: $n = 16$ – Comparator 1: $n = 61$ – Comparator 2: $n = 126$	– Study: embolisation – Comparator 1: surgery (various) – Comparator 2: packing	– Procedural success – Cost – Length of stay – Complications	– Procedural success: study = 75%, comparator 1 = 90%, comparator 2 = 62% – Cost: study = $5697, comparator 1 = $3851, comparator 2 = $5136 – Length of stay: study = 2.6 days, comparator 1 = 2.1 days, comparator 2 = 5.3 days – Complications: study = transfusion (6), tissue ischaemia (1); comparator 1 = transfusion (10); comparator 2 = transfusion (12), alar necrosis (3), angina (1)	Grade: 12 – Small numbers in study group – Retrospective study without follow-up data – Contemporary groups
Strong *et al.*[16] (1995)	– Retrospective study – Single centre, in USA – 10-year data collection period	– Inclusion: refractory posterior epistaxis – Study: $n = 12$, age 60 years (range, 46–84 years), 9M:3F – Comparator: $n = 9$, age 50.8 years (range, 27–76 years), 7M:2F	– Study: embolisation – Comparator: IMA ligation	– Recurrence – Cost – Post-op length of stay	– Recurrence: study = 8.3%, comparator = 44% – Cost: study = $6783, comparator = $5941 – Post-op length of stay: study = 2.7 days, comparator = 3.9 days	Grade: 9 – Small retrospective analysis – Lack of defined follow up – Poorly defined outcome measures

Villwock & Jones[43] (2013)	– Retrospective study – US national database (20% sample of US hospitals) – 3-year data collection period	– Inclusion: epistaxis treated with packing, surgery or embolisation – Exclusions: patients receiving both surgery & embolisation – Study: $n = 1956$ – Comparator 1: $n = 2706$ – Comparator 2: $n = 30\ 389$ – Comparator 3: $n = 21\ 872$	– Study: embolisation – Comparator 1: ligation – Comparator 2: packing – Comparator 3: conservative management	– Length of stay – Charge – Cost – Stroke rate – Mortality	– Length of stay: study = 4.1 days, comparator 1 = 3.9 days, comparator 2 = 3.3 days, comparator = 3.2 days – Charge: study = \$65 707, comparator 1 = \$32 606, comparator 2 = \$19 699, comparator 3 = \$19 914 – Cost: study = \$22 347, comparator 1 = \$11 354, comparator 2 = \$6808, comparator 3 = \$6938 – Stroke rate: study = 1.5 %, comparator 1 = 0.6%, comparator 2 = 0.3%, comparator = 0.1% – Mortality: study = 0.3%, comparator 1 = 1.3%, comparator 2 = 0.7%, comparator 3 = 0.8%	Grade: 17 – Large national study – Useful costing information, though specific to US healthcare
Villwock & Goyal[18] (2014)	See Appendix I					
Wehrli *et al.*[19] (1988)	– Retrospective study – Single centre, in Switzerland – 3-year data collection period	– Inclusion: refractory epistaxis – Study: $n = 18$, 24–81 years (11 males, mean 48.3 years; 7 females, mean 69.5 years) – Comparator: $n = 17$, 39–82 years (11 males, mean 54.6 years; 6 females, mean 73.5 years)	– Study: embolisation (GA) – Comparator: IMA ligation (10), endonasal SPA coagulation (4), endonasal ethmoidal coagulation (2), ECA ligation (1)	– Recurrence – Complications	– Recurrence: study = 22%, comparator = 35% – Complications: study = facial nerve paralysis (2), tissue necrosis (2), temporofacial pain (6), paraesthesia (3), trismus (2), cheek swelling (1); comparator = numbness (2), sinusitis (1)	Grade: 13 – Heterogeneous control group – Group cross-overs – Poorly defined outcome measures
Non-RCTs without comparators						MINORS; max grade of 16
Baloch *et al.*[44] (2012)	– Retrospective study – Single centre, in Pakistan – 10-year data collection period	– Inclusion: epistaxis refractory to packing – Exclusions: nasal or nasopharyngeal mass – $n = 16$, age 51.2 years (range, 26–71 years), 14M:2F	Embolisation of IMA ± additional vessels	– Recurrence – Complications – Length of stay	– Recurrence: 2 (12.5%) – Complications: transient facial pain (1), femoral artery haematoma (1) – Length of stay: 3.9 days	Grade: 6 – Small retrospective study – Short follow-up period
Breda *et al.*[45] (1989)	– Retrospective study – Single centre, in USA – 7-year data collection period	– Inclusion: persistent epistaxis following IMA ligation – $n = 11$, age 56 years (range, 28–78 years), 6M:5F	Embolisation of IMA	– Recurrence – Complications	– Recurrence: 2 (18%) – Complications: soft tissue loss of columella (1)	Grade: 6 – Small retrospective study – Loss to follow up not reported – Unclear if consecutive patients
Christensen *et al.*[46] (2005)	– Retrospective study – Single centre, in USA – 7-year data collection period	– Inclusion: posterior epistaxis treated with embolisation – $n = 70$, age 59.1 years (range, 9–88 years), 41M:29F	Embolisation of IMA ± additional vessels	– Minor recurrence – Major recurrence (requiring surgical intervention) – Late recurrence (>6 weeks post-procedure) – Complications – Hospital charge	– Minor recurrence: 4 (6%) – Major recurrence: 9 (13%) – Late recurrence: 10 (14%) – Complications: stroke (1) – Charge: \$18 000 average	Grade: 6 – Large series – Detailed outcome measures – Reliance on external follow up

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Appendix II *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Cohen *et al.*[47] (2012)	– Retrospective study – Single centre, in Israel – 9-year data collection period	– Inclusion: epistaxis refractory to packing – Exclusions: traumatic, post-op, aneurysm, AVM, radiotherapy, HHT – *n* = 19, age 61 years (range, 29–86 years), 17M:2F	Embolisation of IMA ± additional vessels	– Immediate recurrence – Late recurrence, conservative – Late recurrence, with repeat embolisation – Complications – Post-op length of stay	– Immediate recurrence: 0 (0%) – Late recurrence, conservative: 3 (15.8%) – Late recurrence, with repeat embolisation: 1 (5.3%) – Complications: 0 (0%) – 'transient pain in one third' – Post-op length of stay: 5.2 days (range, 1–13 days)	Grade: 8 Small retrospective study
Duncan *et al.*[48] (2004)	– Retrospective study – Single centre, in South Africa – 4-year data collection period	– Inclusion: epistaxis refractory to packing or cautery – *n* = 51, age 54.4 years (range, 17–83 years), 28M:23F	Embolisation of IMA ± additional vessels	– Recurrence i. Further embolisation ii. Surgical AEA ligation iii. Repeat angiography iv. Other – Complications	Recurrence: 8 (15.7%) i. 4 (7.8%) ii. 2 (4%) iii. 1 (2%) iv. 1 (2%) – Complications: stroke (1), transient headache (3), transient facial pain (2), groin haematoma or pain (4)	Grade: 10 – Strength: clear description of timing of re-bleed cases & their further management – Weakness: telephone follow up, high loss to follow up
Elahi *et al.*[49] (1995)	– Retrospective study – Single centre, in USA – 10-year data collection period	– Inclusion: epistaxis refractory to packing or surgery – *n* = 54, age 53.1 years (range, 12–93 years), 34M:20F	Embolisation of IMA ± additional vessels	– Immediate success – Success after further embolisation – Failure despite supplemental measures – Complications	– Immediate success: 49 (91%) – Success after further embolisation: 52 (96%) – Failure: 2 (6%) – Complications: seizure or stroke (1), transient limb paresis (1), transient infra-orbital numbness (1), transient temporofacial pain 2 (3.7)	Grade: 11 – Large sample of consecutive patients, with clear rationale for treatment strategies – Long average follow up
Elden *et al.*[50] (1994)	– Retrospective study – Single centre, in Canada – 8-year data collection period	– Inclusion: epistaxis refractory to packing (81 emergent, 16 elective) – includes idiopathic, traumatic, tumour & HHT (16.5%) – Exclusions: low platelet count, facial trauma – *n* = 97, age 53 years (range, 12–91 years), 64M:33F	Embolisation of IMA ± additional vessels	– Early recurrence (<1 week) – Long-term recurrence (>1 week) – Complications	– Early recurrence: 11 (11.3%) – Long-term recurrence: emergency cases = 14 (18%), elective cases = 7 (47%) NB. If exclude HHT from analysis, success rate = 90% – Complications: anaesthesia hypoxia or aspiration (1), transient facial pain (20), groin haematoma (3), palate ulceration (1), trigeminal paraesthesia (1), CVA & retinal artery occlusion (1), skin slough or trismus (1)	Grade: 11 – Large series – Clearly defined outcomes – Subgroup analysis of emergent & elective cases for re-bleeding in longer term

Fukutsuji *et al.*[51] (2008)	– Retrospective study – Single centre, in Japan – 10-year data collection period	– Inclusion: epistaxis refractory to nasal packs or surgery – $n = 22$, age 56.8 years (range, 31–76 years), 21M:1F	Embolisation of IMA ± additional vessels	– Short-term recurrence (in-patient) – Long-term recurrence (discharged) – Transient complications (<1 week) – Major complications (>1 week) – Post-op length of stay	– Short-term recurrence: 5 (22.7%) – Long-term recurrence: 1 (4.5%) – Transient complications: facial pain (6), facial numbness (3), headache (2), jaw pain (2), facial oedema (1) – Major complications: 0 (0) – Post-op length of stay: 10.7 days	Grade: 11 – Homogeneous cohort – Clear outcome definitions – Short minimum follow up
Gottumukkala *et al.*[52] (2013)	– Retrospective study – Single centre, in USA – 13-year data collection period	– Inclusion: refractory epistaxis – Exclusions: non-idiopathic epistaxis – $n = 84$, age 63.8 years (range, 26–102 years), 47M:37F	Embolisation of IMA ± additional vessels	– Recurrence (within 30 days) – Complications – Recurrence & complication rate compared to number of vessels embolised: 1 vessel, $n = 8$; 2 vessels, $n = 35$; 3 vessels, $n = 32$; 4 vessels, $n = 9$	– Recurrence: 9 (11%) – Complications: TIA (1), transient lip oedema or slough (1), mild facial or jaw pain (13), mild nasal pain (4), mild headache (3), eyelid oedema (1) – Vessels embolised, recurrence ($p = 0.04$): 1 = 2 (25%), 2 = 5 (14%), 3 = 2 (6%), 4 = 0 (0%) – Vessels embolised, complications ($p = 0.004$): 1 = 0 (0%), 2 = 6 (17%), 3 = 11 (34%), 4 = 5 (56%)	Grade: 10 – Large study – Useful subgroup analysis
Hicks & Vitek[53] (1989)	– Retrospective study – Single centre, in USA – 6-month data collection period	– Inclusion: refractory epistaxis – $n = 7$, age 19–66 years, all male	Embolisation of IMA	– Recurrence – Complications	– Recurrence: 0 (0%) – Complications: transient temporofacial pain (4)	Grade: 5 – Follow-up information lacking – Very small series – Lack of procedural detail
Kordecki *et al.*[54] (2008)	– Retrospective study – Single centre, in Poland – 5-year data collection period	– Inclusion: refractory idiopathic & traumatic epistaxis – $n = 58$, males 24–48 years, females 26–44 years, 39M:19F	Embolisation of IMA ± additional vessels	– Recurrence – Complications	– Recurrence: 9 (15.5%) – Complications: headache (9), facial oedema (3)	Grade: 8 Follow-up methods & drop-out rate unclear
Leppanen *et al.*[55] (1999)	– Retrospective study – Single centre, in Finland – 8-year data collection period	– Inclusion: epistaxis refractory to packing – $n = 37$, age 53 years (range, 20–74 years), 29M:8F	Embolisation of IMA	– Recurrence – Complications – Post-op length of stay	– Recurrence: 4 (11%) – Complications: transient upper limb paresis (1), transient nasal or cheek numbness (3), mortality (1 patient 10 days post-op) – Post-op length of stay: 2 (1–5) days	Grade: 11 Homogeneous cohort

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Appendix II *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Lesley *et al.*[56] (2010)	– Retrospective study – Single centre, in USA – 3.5-year data collection period	– Inclusion: refractory epistaxis treated with embolisation, specifically with use of detachable platinum fibred coils – Exclusions: embolisation with use of particulates, liquid glue or non-permanent embolics – $n = 20$, age 63 years (range, 35–85 years), 13M:7F	Embolisation of uni/bilateral IMA	– Recurrence (30 days) – Complications, $n/20$ (%)	– Recurrence: 1 (5%) – Complications: transient facial pain (1)	Grade: 11 – Strengths: simple, clearly defined outcome measures; homogeneous treatment strategy, with same technique – Weaknesses: small retrospective study; short follow-up period, with telephone follow up
Lopez *et al.*[57] (1998)	– Retrospective study – Single centre, in France – Data collection period not specified	– Inclusion: refractory epistaxis, including secondary to trauma or HHT (unclear proportions) – Exclusions: nasal tumour, AVM – $n = 67$, ages not reported, 46M:21F	Embolisation of uni/bilateral IMA	– Immediate success (bleeding cessation) – Recurrence (within 48 hours) – Complications	– Immediate success: 67 (100%) – Recurrence: 2 (3%) – both HHT patients – Complications: transient pain or trismus (2)	Grade: 6 – Follow up not clearly reported despite high reported success rates – Includes patients with HHT – No information on patient age
Moreau *et al.*[58] (1998)	– Retrospective study – Single centre, in France – 14-year data collection period	– Inclusion: epistaxis refractory to packing including secondary trauma (22%) & HHT (2%) – $n = 45$, age 48.8 years (range, 7–82 years), 3M:1F	Embolisation of IMA ± additional vessels	– Immediate success – Immediate success after successive embolisation – Long-term recurrence – Complications	– Immediate success: 43 (95%) – Immediate success after successive embolisation: 44 (97%) – failure in HHT patient – Recurrence: 6 (13%) – Complications: unilateral blindness (1), transient hemiparesis (1), trismus (1), transient temporofacial pain (1)	Grade: 11 – Heterogeneous cohort (10 patients included were traumatic) – No explanation of inclusion of 7-year-old
Oguni *et al.*[59] (2000)	– Retrospective study – Single centre, in Japan – Data collection period not specified	– Inclusion: refractory epistaxis – Exclusions: HHT, tumour – $n = 37$, age 57.3 years (range, 25–78 years), 31M:6F	Embolisation of IMA ± additional vessels	– Immediate success – Early recurrence (<1 week) – Late recurrence (>1 week) – Complications	– Immediate success: 37 (100%) – Early recurrence: 2 (5.4%) – Late recurrence: 2 (5.4%) – Complications: temporofacial pain (9), headache (7), fever (2)	Grade: 12 – Clearly stated aims – Well-defined outcome measures – Candid reporting of minor complications
Roberson & Reardon[60] (1979)	– Retrospective study – Single centre, in USA – 5-year data collection period	– Inclusion: refractory epistaxis – $n = 10$, age 60 years (range, 29–64 years), 8M:2F	Embolisation of IMA	– Failure – Complications	– Failure: 2 (20%) – both proceeded to surgery – Complications: persistent facial pain (3), temporofacial pain (3)	Grade: 7 – Small series during early evolution of procedure – Narrative results reported on case-by-case basis

Sadri *et al.*[61] (2006)	– Retrospective study – Single centre, in UK	– Inclusion: epistaxis refractory to other treatment modalities (includes post-op, trauma, neoplastic) – $n = 14$, age 57 years (range, 18–95 years), 6M:1F	Embolisation of uni/bilateral IMA	– Recurrence – Complications, $n/14$ (%)	– Recurrence: 4 (29%) – Complications: necrosis of alar skin (1), mucosal necrosis of hard palate (1)	Grade: 9 – Reliance on telephone follow up – Heterogeneous cohort
Scaramuzzi *et al.*[62] (2001)	– Retrospective study – Single centre, in Ireland – 2-year data collection period	– Inclusion: epistaxis refractory to packing (33% traumatic) – $n = 12$, age 51.1 years (range, 21–80 years), 10M:2F	Embolisation of uni/bilateral IMA	– Immediate technical success – Recurrence – Complications	– Immediate technical success: 12 (100%) – Recurrence: 2 (17%) – proceeded to ECA ligation – Complications: transient jaw pain (2)	Grade: 11 – Small retrospective sample – Poor definition of outcome measures (2 patients with post-embolisation bleeding were considered to have 'permanent haemostasis')
Seidel *et al.*[63] (2015)	– Retrospective study – Single centre, in Germany – 7-year data collection period	– Inclusion: epistaxis refractory to conservative or surgical measures – $n = 12$, age 58 years, 9M:3F	Embolisation of uni/bilateral IMA	– Immediate or short-term success – Long-term success – Complications – Post-op length of stay	– Immediate or short-term success: 9 (75%) – Long-term success: ≥6 (≥50%) – Complications: mortality (1 due to ARDS) – Post-op length of stay: 5.1 days	Grade: 9 Follow up clearly defined & reported, but significant loss to follow up in small series
Shah[64] (2008)	– Retrospective study – Single centre, in USA – 2-year data collection period	– Inclusion: epistaxis refractory to nasal packing – $n = 8$, age 65 years (range, 35–90 years), 6M:2F	Embolisation of bilateral IMA ± ipsilateral facial artery	– Recurrence – Complications	– Recurrence: 1 (12.5%) – Complications: transient temporofacial pain (1), re-intubation for airway protection (1)	Grade: 7 – Very small retrospective study – No information on follow-up period
Siniluoto *et al.*[65] (1993)	– Retrospective study – Single centre, in Finland – 6-year data collection period	– Inclusion: epistaxis refractory to packing or surgery (including in trauma, iatrogenic & haematological disease) – $n = 31$, age 49.2 years (range, 18–72 years), 26M:5F	Embolisation of uni/bilateral IMA	– Immediate success – Long-term success (cessation of bleeding, with long-term cure of epistaxis) – Failure – Complications	– Immediate success: 22 (71%) – Long-term success: 20 (64.5%) – Failure: 9 (29%) – 7 proceeded to ethmoid artery ligation – Complications: mortality (2 from primary haematological disease at day 2 & 33 – not attributable to embolisation), temporofacial pain for 24 hours (30)	Grade: 9 Clear description of failed embolisation cases with decision to proceed to ethmoid artery ligation
Strach *et al.*[66] (2011)	– Retrospective study – Single centre, in Germany – 9-year data collection period	– Inclusion: epistaxis refractory to packing or endoscopic coagulation (10% HHT cases) – $n = 48$, age 57 years (range, 14–87 years), 3M:1F	Embolisation of IMA ± additional vessels	– Initial success – Long-term cessation of epistaxis (excluding 5 HHT patients) – Complications – Post-op length of stay	– Initial success: 45 (93.8%) – proceeded to repeat embolisation (1), ethmoid ligation (2) – Long-term cessation of epistaxis: 40/43 (93%) – Complications: necrosis of nasal tip (1), transient hemiparesis ($n = 1$) – Post-op length of stay: 3.9 days (1–18 days)	Grade: 9 – Detailed methodology provided with treatment strategy clearly laid out – Subgroup analysis of iatrogenic epistaxis & HHT patients

Continued

Appendix II *Continued*

Study (year)	Method	Participants	Interventions	Outcome measures	Results	Bias grade/results & assessment details
Strutz & Schumacher[67] (1990)	– Retrospective study – Single centre, in Germany – 3-year data collection period	– Inclusion: epistaxis refractory to packing including trauma (18%), iatrogenic (18%), HHT (9%) – $n = 11$, 5M:6F	Embolisation of IMA	– Recurrence – Major complications	– Recurrence: 2 (18%) – subsequent IMA ligation (1), repeat embolisation (1) – Major complications: 0 (0%) – although muscle pain, trismus & fever reported	Grade: 5 – No medium- to long-term follow-up data – Unclear age of embolisation group
Tseng *et al.*[68] (1998)	– Retrospective study – Single centre, in USA – 5-year data collection period	– Inclusion: refractory epistaxis – $n = 107$, age 55 years (range, 13–88 years), 77M:35F	Embolisation of IMA ± additional vessels	– Immediate recurrence (on pack removal) – Medium- to long-term recurrence (post-discharge) – Overall success – Complications	– Immediate recurrence: 8 (7.5%) – proceeded to ethmoid ligation (7) or packing (1) – Medium- to long-term recurrence: 8 (7.5%) – proceeded to ethmoid ligation (5), repeat embolisation (2) or packing (1) – Overall success: 99 (88%) – Complications: hemiplegia or stroke (2), facial pain (5), mental status changes (5), headache (3), jaw pain (1), facial oedema (1), facial numbness (1), groin pain (1)	Grade: 6 – Large series Short (1 week) follow up for most patients
Vitek[69] (1991)	– Retrospective study – Single centre, in USA – Data collection period not specified	– Inclusion: epistaxis refractory to packing – Exclusions: HHT or traumatic epistaxis – $n = 30$, age 62 years (range, 28–83 years), 21M:9F	Embolisation of IMA ± facial artery	– Failure (continued bleed): embolisation of IMA only; embolisation of IMA & facial artery – Complications	Failure of IMA embolisation: 4 (13%) – all proceeded to facial artery embolisation Failure of IMA & facial artery embolisation: 1 (3%) – resolved with packing – Complications: transient hemiparesis (1)	Grade: 8 – Detailed operative description – Clear rationale of sequential embolisation – Lack of follow-up data
Vokes *et al.*[70] (2004)	– Retrospective study – Single centre, in New Zealand – 5.5-year data collection period	– Inclusion: epistaxis refractory to conservative management – $n = 28$, age 55 years (range, 25–77 years), 18M:10F	Embolisation of IMA ± additional vessels	– Initial success – Complications, $n/28$ (%) – Length of stay	– Initial success: 24 (86%) – Complications: groin haematoma (2), headache (1), jaw pain (1), visual changes (temporary) (1), numbness in distribution of CNV2 & trismus (1) – Length of stay: 5 days (1–7 days)	Grade: 9

RCT = randomised controlled trial; MINORS = methodological index for non-randomised studies; M = male; F = female; IMA = internal maxillary artery; AEA = anterior ethmoidal artery; ICA = internal carotid artery; MI = myocardial infarction; post-op = post-operative; HHT = hereditary haemorrhagic telangiectasia; GA = general anaesthesia; SPA = sphenopalatine artery; ECA = external carotid artery; AVM = arteriovenous malformation; CVA = cerebrovascular accident; TIA = transient ischaemic attack; ARDS = acute respiratory distress syndrome; CNV2 = maxillary nerve