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REVIEW

Selective embolisation for intractable bladder haemorrhages: A systematic review of the literature

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KEYWORDS

Intractable bladder haemorrhage (IBH);
Selective transarterial embolisation (STE);
Conservative treatment;
Urinary tract infection (UTIs)

ABBREVIATIONS

IBH, intractable bladder haemorrhage;

Abstract ***Objective:*** To establish the current evidence and assess the effectiveness and safety of selective transarterial embolisation (STE) to control intractable bladder haemorrhage (IBH).

Materials and methods: With a rise in the use of STE for the treatment of IBH, a systematic review was performed according to the Cochrane reviews guidelines and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

Results: The literature search yielded 38 studies, of which 11 were excluded because of irrelevance of data. All included studies were observational cohort studies, with no randomisation or control groups apart from in relation to the materials used for embolisation. The studies were published between 1978 and 2016. There were 295 patients with an age range between 51 and 95 years. The success rate ranged from 43% up to 100%. The most reported complication was post-embolisation syndrome, although

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MeSH, Medical Subject Headings; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; STE, selective transarterial embolisation

other complications were described such as mild transient gluteal claudication, nausea, and vomiting.

Conclusion: STE of the internal iliac artery is a safe and effective alternative technique to control severe IBH, and has been successfully applied over many years to treat bladder haemorrhage associated with terminal pelvic malignancy.

Introduction

Intractable bladder haemorrhage (IBH) is a rare urological emergency that can potentially be life-threatening and its management difficult. It is a comorbid serious condition and associated with increased admissions and transfusions. IBH can arise as a result of radiation cystitis, bladder carcinoma, cyclophosphamide-induced cystitis, severe infection, or locally advanced prostate cancer [1–3].

The management of IBH is difficult and may necessitate interventional radiology to embolise main vessels to stop the bleeding. Selective transarterial embolisation (STE) of the internal iliac artery is a palliative measure to control bleeding. Numerous studies have shown the STE leads to a cessation of bleeding with low associated morbidity [1–3].

Despite the reported success, the only available evidence for STE has been case series. To this end, we aimed to conduct a systematic review of the literature to establish the current evidence and assess the effectiveness and safety of STE to control IBH.

Materials and methods

Search strategy and study selection

The systematic review was performed according to the Cochrane reviews guidelines and in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [4].

The search strategy was conducted to find relevant studies from Medline (1966–2017), EMBASE (1980–2017), Google Scholar and individual urological journals. The search was conducted in April 2017.

The search terms used included: 'bladder', 'cystitis', 'haemorrhage', and 'bleeding', 'embolisation' and 'haematuria'. The Medical Subject Headings (MeSH) phrases included: ('Urinary Bladder' [MeSH]) AND 'Haemorrhage' [MeSH]).

(('Urinary Bladder' [MeSH]) AND 'Haemorrhage' [MeSH]) AND 'Embolization, Therapeutic' [MeSH]).

(((('Urinary Bladder' [MeSH]) AND 'Haemorrhage' [MeSH]) AND 'Embolization, Therapeutic' [MeSH]) AND 'Arteries' [MeSH].

All papers irrespective of language were included if they reported on STE. The references of the identified papers were evaluated for potential inclusion. Authors of the included studies were contacted whenever the data were not available or not clear.

Two reviewers (D.E.T. and O.A.A.) identified all the studies that adhered to the inclusion criteria for full review. Each reviewer independently selected studies for inclusion. Disagreement between the extracting authors was resolved by consensus or referred to the third author (A.A.S.).

Data extraction and analysis

The objectives were to evaluate the effectiveness and safety of STE for IBH. The following variables were extracted from each study: patient demographics, blood loss, transfusion rates, duration of hospital stay, procedure success rate to stop bleeding, and complications that were classified according the Clavien–Dindo classification system [5]. The data from each study were grouped into a meta-analysis, in an intention-to-treat basis, to allow a numerical representation of the results.

Results

The literature search yielded 38 studies, of which 11 were excluded because of the irrelevance of the data (Fig. 1). The titles and abstracts of the studies did not give sufficient data on IBH; hence, their exclusion.

Full manuscripts were evaluated in 11 of 27 studies that were included in the review [1,6–15]. All included studies were observational cohort studies, with no randomisation or control groups, apart from in relation to the materials used for embolisation and reported on IBH. Three studies were case reports [16–18].

All studies that reported on the variables indicated in the data extraction section are shown in Table 1.

Characteristics of the included studies

The studies were published between 1978 and 2016. There were 295 patients, with an age range between 51 and 95 years.

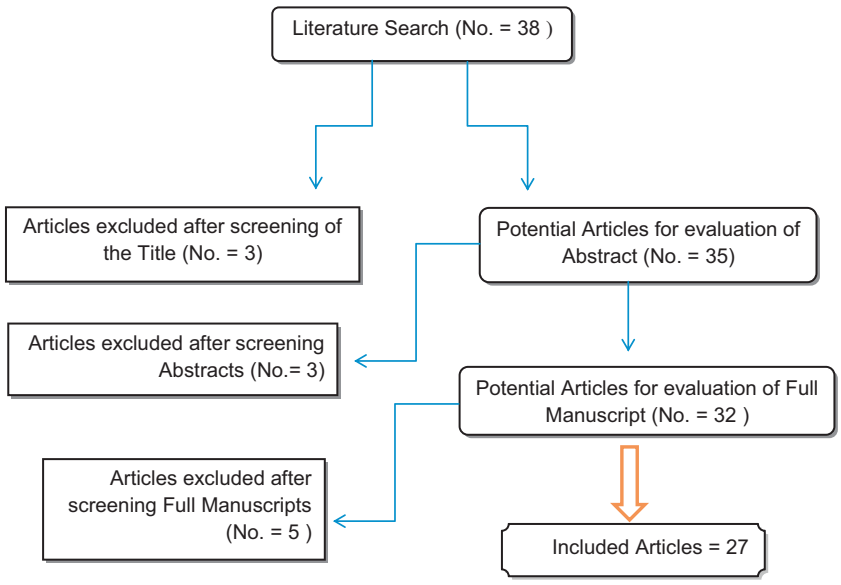

Fig. 1 Flowchart of article selection.

For the main outcome of effectiveness, nine studies reported on the success rate of embolisation, and eight studies reported on complications; however, Ozono et al. [19] reported on the reduction in tumour size and stage reduction, and two studies reported on the difference in outcome between different embolisation materials [20,21].

Various conditions including urogenital pelvic malignancies, radiation cystitis, chemotherapy-induced haemorrhagic cystitis, and UTIs, can trigger IBH [24].

Effects of intervention

The definition of success differed between studies. Some studies defined success as control and no recurrence of haematuria, with the success rate ranging from 43% [10,13] up to 100% [1,15,22]. Korkmaz et al. [15], subdivided the success rate into clinical success, control of haematuria, and technical success. The technical success rate reached 88%, whilst the clinical success rate reached 100%. Pisco et al. [23] subdivided success into 'complete', 'partial response', and 'no response' depending on the need for daily transfusions. Ozono et al. [19] categorised success according to reduction of tumour size (56.7%), tumour down-staging (72.7%), and haemostatic effect (76.5%).

Some studies focused on the need for blood transfusion as an indicator of success [22], whilst others focused on haemoglobin and haematocrit levels [15]. Halpenny et al. [22] reported that the mean transfusion requirement was 8.6 units before embolisation and 0.3 units after embolisation. Liguori et al. [13] reported that of 24 patients (55%) who required a mean (range) of 4 (1–17) transfusion units before STE; only 13 (30%) required more blood products after STE. The mean haematocrit level before and after STE, and the respective haemoglobin levels were significantly different ($P < 0.001$). A second STE session was required in five (11%) patients, and was successful in two of them.

Mortality rates were not a focus in most studies. Liguori et al. [13] reported 6- and 12-month mortality rates of 66% (29 patients) and 18% (eight), respectively. Rodríguez-Patrón Rodríguez et al. [2] reported that four patients died, three of them without haematuria; one because of an intercurrent disease, and the others from disease progression.

Complications

The most reported complication was post-embolisation syndrome [13,23]. Some complications were reported specific to the vessel approached. Rodríguez-Patrón Rodríguez et al. [2] reported a mild transient gluteal claudication when using the inferior mesenteric approach. Minor complications included gluteal pain, nausea, vomiting, and fever in five patients [15].

Discussion

IBH in the context of bladder cancer is a disastrous condition. Most patients in this situation are elderly and unfit, and therefore unlikely to withstand morbid procedures. Those not suitable for curative treatment still have to face the diverse consequences of haematuria.

Various conditions including urogenital pelvic malignancies, radiation cystitis, chemotherapy-induced haemorrhagic cystitis, and UTIs, can trigger IBH [24]. Bladder irrigation, Helmstein balloon compression, and cystoscopic clot evacuation are amongst the most conservative methods used to treat IBH.

Table 1 Details of the 27 studies included in the review.

Authors	Journal/year	Patients, *n*	Follow-up, months	Embolic agent	Bilateral embolisation, % or *n*/*N*	Super-selective embolisation, % or *n*/*N*	Clinical success,% or *n*/*N*	Technical success,% or *n*/*N*	Complications
Anand et al. [18]	*Clin Oncol (R Coll Radiol)*/1991	1	NA	NA	NA	NA	Bilateral internal iliac embolisation		Re-embolisation after 5 months
Thon et al. [17]	*Urologe A*/1984	1	NA	NA	NA	NA	Internal iliac embolisation		
Thelen and Brühl [16]	*Rofo*/1978	5		NA	NA	NA			
Korkmaz et al. [15]	*Diagn Interv Imaging*/2016	18	18	Polyvinyl alcohol particles (300–500 μm in diameter)	NA	NA	100	88	Gluteal pain, nausea, vomiting, and fever in 5 patients
Halpenny et al. [22]	*JBR-BTR*/2013	3	6–13	Gelfoam	NA	NA	3/3		No
Liguori et al. [13]	*BJU Int*/2010	44	10	Polyvinyl alcohol particles (150–700 μm diameter)	100	100	82	100	Post-embolisation syndrome in 12 (27%) patients, fever in 5 (11%), gluteal pain in 6 (14%), nausea in 1 (2%) exterior genital oedema in 2 (5%) late re-bleeding in 22 (50%)
Palma Ceppi et al. [34]	*Actas Urol Esp*/2008	6	NA	Microparticles or coils			4/6 are successful 2/6 cases needed secondary procedure		No
El-Assmy and Mohsen [10]	*Scientific WorldJournal*/2007	7	6–12	Coils			4/7 1 needed re-embolisation after 2 months		No
Nabi et al. [1]	*BJU Int*/2003	6	22	Permanent coil	6/6	0	83.3	6/6	Minor complications, e.g. nausea, vomiting or fever
Rodríguez-Patrón Rodríguez et al. [2]	*Arch Esp Urol*/2003	8	NA	Coils and particles	NA	NA	NA	NA	1 patient referred mild transitory gluteal claudication
Li [35]	*Zhonghua Wai Ke Za Zhi*/1990	16	NA	NA	NA	NA	Successful in 15/16	NA	No
Pisco et al. [23]	*Radiology*/1989	108	6	Permanent coils	100	0	76.8	92.6	70 patients had post-embolisation syndrome 3 had transient acute tubular necrosis Late re-bleeding in 26

Table 1 (*continued*)

Authors	Journal/year	Patients, *n*	Follow-up, months	Embolic agent	Bilateral embolisation, % or *n*/*N*	Super-selective embolisation, % or *n*/*N*	Clinical success,% or *n*/*N*	Technical success,% or *n*/*N*	Complications
Ozono et al. [19]	*Eur Urol*/1988	70	NA	Microencapsulated mitomycin C, gelatine sponge and lipiodol (iodised oil)	NA	NA	Reduction of tumour size in 56.7% Stage reduction in 72.7% Haemostatic effects in 76.5%.	100	Fever, leucocytosis, urinary frequency and pain
Granov et al. [36]	*Vestn Khir Im I I Grek*/1985	30	NA	Use metallic spiral, combined with gelatine sponge	NA	NA	NA	NA	NA
Darewicz [37]	*Int Urol Nephrol*/1983	4	NA	NA	NA	NA	Internal iliac embolisation	NA	NA
McIvor et al. [38]	*Clin Radiol*/ 1982	2	NA	NA	NA	NA	The left axillary approach was used	NA	Gluteal pain
Weber and von Allesch [21]	*Urologe A*/ 1981	9	NA	Particulate Fibrospum and Tachotop and semi-liquid aminoacid-Ethibloc	NA	NA	9/9	NA	No
Kobayashi et al. [29]	*Radiology*/ 1980	2	NA	NA	NA	NA	2/2 unilateral embolisation of vesical artery	NA	No
Carmignani et al. [28]	*Rofo*/1980	9	12 or until death		9/9	0	8/9	9/9	Late re-bleeding 2
Carmignani et al. [39]	*J Radiol*/1979	9	12 or until death		9/9	0	8/9	9/9	Late re-bleeding 2
Giuliani et al. [20]	*Br J Urol*/ 1979	2	NA	Gelatine foam and isobutyl-2cyanoacrylate (IBC)	NA	NA	2/2	NA	No
Kelemen et al. [40]	*Diagn Imaging*/1979	8	NA	NA	NA	NA	8/8	NA	No
Gujral et al. [9]	*Postgrad Med J*/1999	9	NA	NA	NA	NA		NA	NA
Hayes et al. [41]	*Br J Urol*/ 1996	NA	NA	NA	NA	NA	NA	NA	NA

(*continued on next page*)

Table 1 (*continued*)

Authors	Journal/year	Patients, *n*	Follow-up, months	Embolic agent	Bilateral embolisation, % or *n*/*N*	Super-selective embolisation, % or *n*/*N*	Clinical success,% or *n*/*N*	Technical success,% or *n*/*N*	Complications
Lang et al. [42]	*J Urol*/1979	14			14/14	2/14	12/14	14/14	Late re-bleeding 2
Appleton et al. [27]	*Br J Urol*/1988	10	NA	NA	4/10	0	7/10	10/10	Late re-bleeding 2
Rastinehad et al. [31]	*Urology*/2008	10	20	NA	10/10	10/10	10/10	10/10	Late re-bleeding 1

STE of the internal iliac artery is an alternative technique used to control severe haematuria, and has been successfully applied over many years to treat bladder haemorrhage associated with terminal pelvic malignancy [12,25]. This pelvic endovascular procedure is usually performed using local anaesthesia with a digital subtraction angiography unit. Retrograde percutaneous catheterisation of the femoral artery is performed, on one or two sides, using a 5- or 6-F sheath. Then, selective angiography of the internal iliac arteries is performed routinely using a 5-F Cobra or Simmons-type 2 catheter to delineate the pelvic arterial anatomy. Vesical and prostatic arteries can arise as discrete branches of the anterior division of the hypogastric artery, as previously mentioned, as well as branches from the pudendal arteries in men and from the uterine arteries in women.

Abnormal hypervascularity or even a mass may be seen at angiography, but visualisation of extravasation is unusual. Based on angiographic findings superselective catheterisation of the vesical or prostatic branches is routinely done using a 3-F coaxial microcatheter. A schematic drawing of the different origins of the vesical and prostatic arteries is shown in Fig. 2.

Flow-directed embolisation is usually achieved using the preferred embolic agent. In patients with angiographic evidence of contrast extravasation, a sign of active bleeding, distal embolisation of the feeding branch can be done. The embolic material is mixed with ultrafluid lipiodol in a 1:3 ratio to make the embolisation material radiopaque. Occasionally, when the vesical or prostatic arteries cannot be selectively catheterised, coil blockade is used. Coil blockade is performed using 0.0457 cm (0.018-inch) fibred or soft platinum microcoils of various lengths and diameters [9]. The different techniques of embolisation are summarised in Fig. 3.

Various embolic materials have been used over time, such as coils, particles, embospheres, gelatine foam, isobutyl-2-cyanoacrylate, microencapsulated mitomycin C, gelatine sponge, and lipiodol (iodised oil). The current preferred embolic agent is a permanent type, such as calibrated tris-acryl gelatine microspheres. With gelatine sponge particles re-canalisation may develop after 2–3 weeks [12]. Polyvinyl alcohol (PVA) particles of 30 0–500 μm in diameter have been used for distal embolisation, whilst particles of 500–700 μm in diameter can be injected to embolise more proximal abnormal vessels. Coil blockade is performed using 0.0457 cm (0.018-inch) fibred or soft platinum microcoils of various lengths and diameters [26]. The influence of the type of embolic agent on clinical outcomes is controversial. In most series the number of patients was too small to allow conclusions about the best embolic agents [9,26,27].

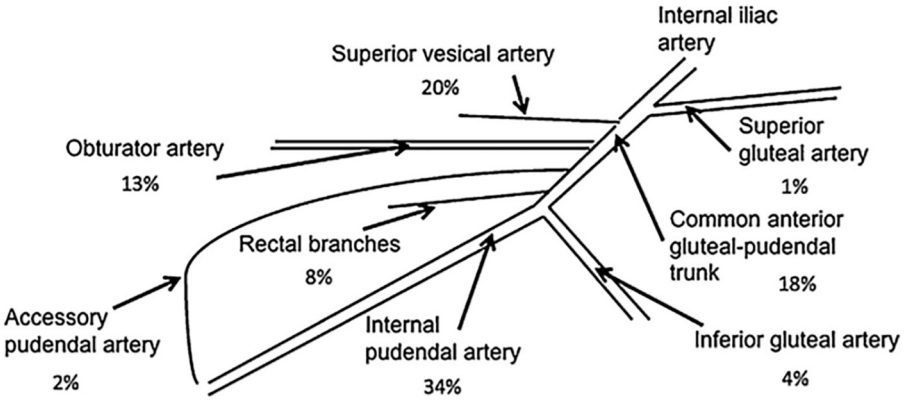

Fig. 2 Schematic drawing of the different origins of the vesical and prostatic arteries.

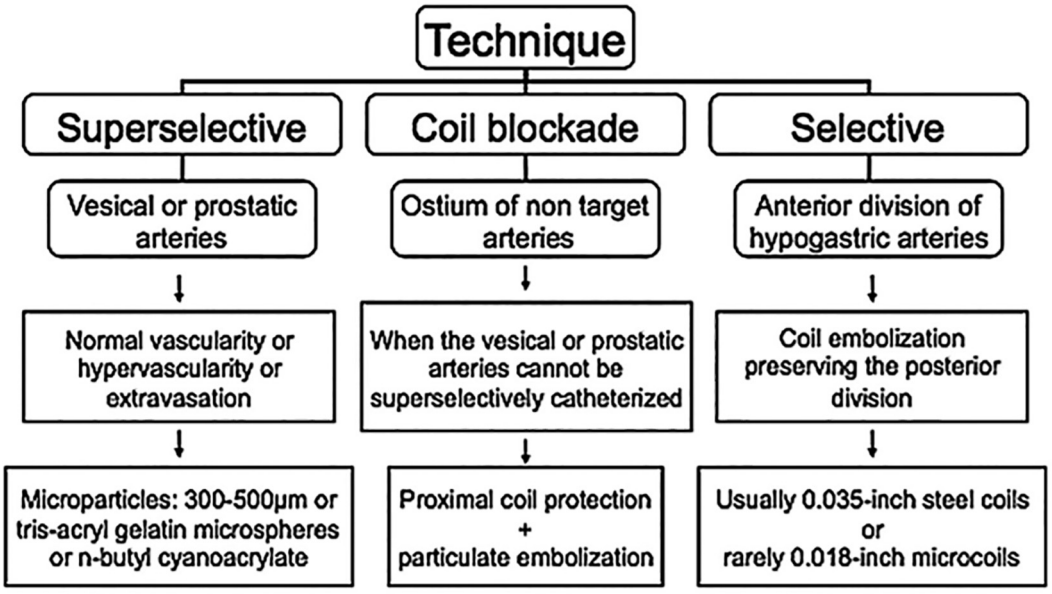

Fig. 3 Main techniques of bladder or prostate angiographic embolisation: super-selective embolisation, coil blockade technique, and selective embolisation.

The most reported complication was post-embolisation syndrome [13,23]. Post-embolisation syndrome involves nausea, vomiting, gluteal pain, and fever due to tissue necrosis. It can be managed conservatively with symptomatic medications. Transient acute tubular necrosis also is a common reported complication, caused by contrast medium. Other side-effects can occur, e.g. fever, gluteus pain, nausea, and exterior genital oedema [15]. Some complications were reported specific to the vessel approached, e.g. mild transient gluteal claudication when using the inferior mesenteric approach [2]. Brown-Sequard's syndrome can occur because of the presence of anastomoses between the vesical arteries and the sacral lateral arteries, which has to be checked during angiography, bladder necrosis, gluteal paresis or skin necrosis [23,27–30].

Superselective embolisation of the bladder or prostate arteries should be performed whenever possible to minimise the risk of ischaemic complications at other sites of the internal iliac territory. It has lower complication rates of ~10% [26,31].

Embolisation can be done either unilaterally or bilaterally. Earlier studies suggest a higher risk of re-bleeding after unilateral embolisation [32,33]. Re-bleeding after unilateral embolisation is probably related to the rich collateral blood supply to the internal iliac artery from the contralateral internal iliac, inferior mesenteric, external iliac, and femoral arteries. To prevent re-bleeding from these collaterals the anterior division of the internal iliac artery should probably be embolised bilaterally regardless of whether the bleeding site is detectable on angiogram [1,19,23,31].

Of course, the mortality rate and follow-up after embolisation are usually relatively high and short in most studies, respectively, as the target population is composed mostly of elderly patients with advanced malignancy [26,31]. Mortality may be due to intercurrent disease and for others disease progression [2]. However, mortality is rarely due to re-bleeding and embolisation can obviate the need for radical surgery. The 6- and 12-month mortality rates were 66% and 18%, respectively [13].

Conclusion

STE of the internal iliac artery is a safe and effective alternative technique to control severe IBH, and has been successfully applied over many years to treat bladder haemorrhage associated with terminal pelvic malignancy.

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Conflicts of interest

None.

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None.

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