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Effectiveness of embolization or sclerotherapy of pelvic

veins for reducing chronic pelvic pain: a systematic

review

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Disclosure of Interests

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Abstract

Purpose

Chronic pelvic pain (CPP) in the presence of dilated and refluxing pelvic veins is often described as pelvic congestion syndrome (PCS), although the causal relationship between pelvic vein incompetence and CPP has not been established. Percutaneous embolization is the principal treatment for PCS, with high success rates cited. Our objective was to systematically and critically review the effectiveness of embolization of incompetent pelvic veins.

Materials and Methods

A comprehensive search strategy encompassing various terms for pelvic congestion, pelvic pain and embolization was deployed in 17 bibliographic databases, with no restriction on study design. Methodological quality was assessed. The quality and heterogeneity generally precluded meta-analysis. Results were tabulated and described narratively.

Results

21 prospective case series and one poor quality randomized trial of embolization (involving 1308 women) were identified. Early substantial relief from pain was observed in approximately 75% of women undergoing embolization, which generally increased over time and was sustained. Where pain was measured on a visual analogue scale, statistically significant reductions following treatment were observed in all studies. Re-intervention rates were generally low. There were few data on the impact on menstruation, ovarian reserve or fertility, but no concerns were noted. Transient pain was common following foam embolization, whilst there was a <2% risk of coil migration.

Conclusions

Embolization appears to provide symptomatic relief of chronic pelvic pain in the majority of women and is safe, although the quality of the evidence is low.

Introduction

Pelvic congestion syndrome (PCS) is described as chronic pelvic pain arising from dilated and refluxing incompetent pelvic veins. The diagnosis is based on patient reported symptoms, clinical examination, anatomical features, and venographic findings. There are no generally accepted, well-defined clinical criteria for the diagnosis of PCS, reflecting the residual uncertainty that there is a causal relationship between pelvic vein incompetence (PVI) and chronic pelvic pain (CPP).

Elimination of the blood flow is a recognized strategy for treating incompetent veins. This can be achieved surgically, by ligation of a vein or since the early 1990s, via percutaneous introduction of an embolic agent upstream downstream of the dilated or refluxing veins.(1) Once the incompetent vein is occluded, blood is diverted via other veins, and in time, new vessels can form in the place of the original, although in theory these too could become incompetent. Whether recurrence of symptoms is a result of failure of the original embolization, or due to collateral or recanalized veins diverting the flow to the internal iliac vein (IIV) or elsewhere, , or through untreated or *de novo* varices, is unclear.

The objective of this systematic review of the literature was to assess the effectiveness of percutaneous embolization of incompetent pelvic veins in reducing CPP in women. Secondary objectives were to assess radiological features, impact on fertility and adverse events.

Materials and methods

The systematic review was conducted based on a protocol developed prior to commencing the review and it has also been registered with the PROSPERO database. Ethics approval was not needed as no patients or patient identifiable data were involved.

Search strategy

A comprehensive search strategy was developed. This was used in the following bibliographic databases: Web of Knowledge, British Nursing Index, CINAHL, Cochrane Library, DARE, Embase, MEDION, Medline and Web of Science. The foreign databases, AIM, IMEMR, IMSEAR, LILACS, PAHO, Popline, SciELO and WPRIM held on the World Health Organisation portal were also searched, from database inception to November 2013. Bibliographies of all relevant primary articles and reviews were hand searched to identify articles missed by the electronic searches. No language or study design restrictions were applied in the searching phase.

Search terms for the condition included pelvic pain, pelvic congestion, pelvic or ovarian vein, incompetence or reflux, and variations of these as keywords and text. Search terms for the intervention included treatment, endovascular therapy, interventional radiology, embolization, sclerotherapy, ligation or occlusion, and variations of these as keywords and text. Wild card characters were used to capture alternative spellings and stems of words. The condition and treatments terms were each combined using the "or" term to broaden the search and the two components combined using the "and" function. See *Supplementary Appendix 1*.

Study selection and data extraction

Studies were selected for inclusion in the review in a three-step process (see Figure 1) if they fulfilled the following criteria:

1. Population: Women with a clinical diagnosis of PCS and/or radiological diagnosis of PVI, with or without CPP. No restriction was placed on any previous treatment, age of the participants, duration of symptoms, co-morbidity (including co-presence of endometriosis or other gynecological cause) or severity of the complaint in selection of the studies or on the method of identification of the pelvic varices to be embolized.

- 2. Interventions: Coil embolization or sclerotherapy of pelvic veins, using any method.
- Outcomes: Studies reporting subjective assessment of pain or improvement in pain symptoms.
- 4. Study design: Ideally, only reports of well designed, randomized controlled trials would be included, but preliminary searching indicated that these would be scarce. Primary reports of observational studies were therefore included, but restricted to those where participants were recruited prospectively. Case reports or small series with fewer than 6 participants were excluded. Where it was ambiguous as to whether the data was collected prospectively or retrospectively, a judgement was made based on the timeframe of the follow-up assessments. Where participants were reassessed at particular time-points, it was accepted that they were recruited into the study prospectively. If the duration of follow-up was reported as a wide time frame, it was assumed that participants had been identified retrospectively and the follow-up was a cross-sectional survey, therefore were excluded.

Methodological quality assessment

All studies selected for inclusion were assessed for their methodological quality in duplicate. For any eligible randomized trials, the Cochrane Collaboration risk of bias tool was used.(2) There are no universally accepted quality criteria and reporting standard for case series, as systematic reviews usually tend to exclude studies of this design, and there are no reporting standards. The quality of case series was assessed using criteria adapted from a published checklist.(3),

Data synthesis

Standard meta-analytical methods were used to estimate the overall proportion with a symptomatic improvement following embolization, using the proportions reported in

individual studies under both fixed and random effects assumptions. Plots were generated in MedCalc software (version 14.10.2. Ostend, Belgium). For other outcomes, studies were extracted in duplicate, tabulated and described narratively.

Results

Studies selection for the review

A total of 2858 citations were identified through the electronic bibliographic database searches. Of these 2718 were excluded after reading of titles and abstracts, mainly because they referred to varicose veins of the lower limbs. From 140 citations whose full papers were retrieved, further exclusions were made: seven studies investigated pelvic vein ligation, three studies were considered retrospective but reported on medium to long term outcomes, so were considered for this outcome, (4-6) and two studies, with a total of 37 women, although prospective in design, reported only on technical success and complications.(7, 8) This left 22 studies,(5, 9-29) reporting on 1308 women. A summary of the characteristics of the included studies is given in *Table 1*.

Description of study characteristics

The mean age of the study population was reported in 20 of the studies (5, 9-16, 18-23, 25-29), and ranged between 32 and 51 years,.. Sixteen studies reported the reproductive status of the treated women in some format, (9-12, 14, 18-23, 25-29) usually as the mean parity, which ranged from 0.9 to 3.5. See *Supplementary Table S1*. There was no consistent reporting of any other demographic data e.g. body mass index, history and duration of symptoms.

Bilateral embolization was conducted on 478 women, whilst 384 had only left-sided embolization, six only right-sided embolization, whilst for 440 women it was unclear. The total number of veins embolized and number or proportion of women who had either ovarian or internal iliac vein embolized is indeterminable. One of the larger series of 218 women (23), reported the distribution of the 526 veins treated as 27% right IIV, 23% left IIV, 7% right OV and 32% left OV, but the degree of multiple vein embolization could not be extracted from the study report.

Embolization of pelvic veins was achieved using a sclerosant in 229 women, by use of metal coils (stainless steel or platinum) in 660 women and a combination of both in 405, with the method unclear in the remaining 13 women. The sclerosant used varied considerably and included 1-3% sodium tetradecyl sulphate, (12, 15, 22, 24) 2-3% aetoxisclerol (17, 20, 25, 27) or enbucrilate.(9, 28) There was no apparent trend towards or away from using either technique, either over time or between countries.

Quality assessment

There were 20 case series included in the review, see *Supplementary Tables, Table S2* with one further study being unable to be reliably assessed due to uncertainty after translation.(24) Whilst the aims and embolization techniques were clearly stated, a third did not clearly describe the intended outcome measures and how they were to be collected. Although we sought only prospective trials, it was still not clear in 40% that consecutive patients were included: this was reinforced by poor descriptions of the criteria with which women were referred for venography and inadequate reporting of losses to follow-up.

The sole randomized trial was likely to be subject to selection, performance, measurement and attrition biases and was deemed of low internal validity.

Symptomatic Improvement

Subjective symptom relief was reported on ordinal scales of complete, moderate/ partial or no relief of CPP symptoms in six studies.(9-12, 24, 28) Early reporting of complete symptom relief, less than two months, ranged from 33% (24) to 80% (12) of study participants.)Pooling rates of complete, excellent or moderate improvement from these studies gave an overall improvement rate of 75% (95%CI 64 to 85%, I² statistic 42%) at 4-8 weeks post-procedure. See Figure 2.

Few studies reported symptoms at two time-points. Van der Vleuten *et al* assessed all women twice and found 67% of women had moderate or obvious improvement at two months post-operatively, which increased to 76% at an average of 18 months (+/- 12 months) later.(10) Other studies report 85% of women had some symptom improvement at 6 months (17, 25), which again increased to 95% after 12 months in the smaller study (Tropeano *et al*). At an average of 45 months of follow-up, relief rates of over 80%

were reported by two studies (16, 21) but sustained relief in only 47% in a third study.(26)

Studies reported treatment failures either as residual symptoms, unsatisfactory improvement or as the number of repeat embolizations performed. In a larger study, 22 of 193 of women (11%) had mild or moderate residual symptoms at 6 weeks (23), whilst another reported only 2.2% found their improvement unsatisfactory.(24) Reintervention by 3-6 months due to unresolved symptoms was reported in 5.7% of women by D'Archambeau *et al* (5), lower than the 15% at 3 months cited by Tropeano *et al*.(25)

No study reported quality of life using a generic instrument. Chung and Huh *et al* deployed a social readjustment rating scale (30) to compare stress between women who had embolization or hysterectomy but found no significant differences.(14)

Pain Scores

Nine studies report on pelvic pain scores from 0-10cm visual analogue scales, although at varying time-points after embolization.(13, 14, 16, 18, 19, 22, 25, 26, 29) In all cases, the pain score reduces significantly from a baseline and were generally sustained in those trials. See Figure 3.

Five studies undertook paired t-tests of pain scores before and after embolization and reported the reductions as being statistically significant, with sufficient data that this could be verified by the reviewers.(16, 18, 22, 26, 29) There were insufficient studies with all necessary data to perform a meta-analysis. See *Supplementary Tables, Table S3*.

Several studies reported on different pain symptoms. Kim *et al* noted statistically significant score reductions in pain on standing, lying down, dyspareunia and dysmenorrhea, as well as the amount of pain relief required, (16) whilst Venbrux *et al* also observed similar reductions in all symptoms except dysmenorrhea.(13) Gandini *et al* reported statistically significant reductions in dyspareunia and dysmenorrhea (22); Creton *et al* also considered pain at the site of pelvic varices occurring specifically before or during menstruation, which decreased from a mean of 6.0 to 1.7 at 45 days post embolization and remained low.(19) Van der Vleuten *et al* reported on the widest

range of symptoms, observing statistically significant improvements in scores at 2 months and an average of 18 months (SD 12 months) for dysmenorrhea, dyspareunia, worsening of symptoms with walking, standing or sitting, varicose veins and pain in varicose veins.(28)

Impact on pelvic vein reflux and diameter.

Only two studies quantified the diameter of the pelvic veins before and after the procedure. One study measured the mean diameter of varices in supine patients, decreasing from 6.3 mm to 4.4mm and 4.5mm to 3.1mm for the left and right OV respectively, both statistically significant reductions.(15) In another study, left and right OV diameters reduced from a mean of 6.9mm (SD 2.1) and 5.1mm (SD1.4) to less than 4.5mm on both sides in all cases.(27) Pieri *et al* noted that symptoms persisted in women in whom, although their OV varicosities decreased in diameter from preprocedure measurements, remained over 5mm at rest.(15)

Ratnam *et al* was able to perform a repeat transvaginal ultrasound (TVUS) at 6-8 weeks in 193 patients, observing residual mild reflux in 16 (8.3%).(23) Nine women had a second procedure dictated by the ultrasound: six patients due to moderate persistent reflux and three because of new reflux. Tropeano *et al* also repeated the TVUS at 3, 6 and 12 months and observed an absence of reflux and reduced (<5mm) pelvic vein diameter in 17 of 20 (85%) women.(25) The remaining 3 women who showed recurrence or persistent left sided reflux, were also those who did not report a symptomatic improvement, and had a successful repeat procedure performed at 4-5 months and were reported as symptom free after a median follow-up of 15 months.

Impact on future fertility, menstruation and ovarian reserve

Venbrux *et al* captured information on menstruation between 6 and 24 hours post-procedure, in 24 of 56 participants, finding no significant difference in the interval or length of menstruation compared to before the embolization.(13) Kim *et al* measured follicular stimulating hormone, estradiol, and luteinizing hormone at baseline, six and 12 months and reported no statistically significant differences before and after the procedure.(16)

No study explicitly included or excluded women based on their desire for a future pregnancy, nor specifically mentioned active follow-up of future pregnancies. Therefore, reports of pregnancies are likely not to have been systematically collected. Three studies report six successful pregnancies.(9, 13, 16)

Adverse events of embolization

Six studies did not report any adverse events in their population, although it is not clear whether this equates to technical success in all cases. Of the remaining 938 women, in total there were 10 cases of vein perforation causing extra-vascular leakage of contrast media during the insertion of coils. Transient pain following the embolization was reported in between 8% and 100% of cases and only appeared to occur in the studies using sclerotherapy, with or without coils. One large study of 239 women described early adverse symptoms as a "post-embolization syndrome", reporting that 129 (54%) had transient gluteal or lumbar pain, 61 (26%) general achiness, 30 (12%) transient fever (≥38°C) and 21 (9%) had mechanical superficial phlebitis at the point of venous access in the arm.

Coil migration after placement was reported in 11 cases, being displaced to the lung in eight cases, the renal vein in two cases and one report of coil protrusion into the femoral vein. In all cases, the coil was retrieved by a catheterized snare without any lasting harm to the woman.

Discussion

This systematic review of embolization for PVI found no high quality studies, so all estimates of effectiveness are derived from presumed prospective case series reporting on 1308 women, the majority of whom were of reproductive age and parous.

Early substantial relief from pain symptoms was observed in approximately 75% of 162 women in six case series, which generally increased over time and was sustained. Where pain was measured on a visual analogue scale, statistically significant reductions following treatment were observed in all studies. Re-intervention rates were generally low. Where measured, embolization reduced the diameter of dilated veins to a significant degree, with minimal residual reflux.

There was little data on menstruation, ovarian reserve or fertility, but no concerns were noted. Transient pain was a common occurrence following foam embolization, whilst there was a <2% risk of coil migration.

The review followed a registered protocol and focused on a clear question for the assessment of effectiveness. The comprehensive search strategy is the broadest ever applied in a review of PCS. All outcomes identified *a priori* were reported upon to the extent that data were available. The embolic techniques employed were generally well described and follow-up data was available for the majority of participants.

The most significant limitation, which prevents firm conclusions being drawn from the data and recommendations being made, is the quality of the studies identified. There is only one randomized controlled trial of embolization in the literature, with hysterectomy as a comparison, which was in itself not free of potential biases. The majority of the studies were relatively small case series, with the inherent high risk of bias, with no comparative group and frequently ill-defined inclusion criteria. In comparison to other reviews in this area, we attempted to restrict the studies included to those where participants were prospectively enrolled, in order to reduce selection bias, unlike other reviews.(31). However, in some studies it was impossible to be completely certain, from the methodology used, that included participants were not retrospectively identified from medical records.

The effect of embolization on pain was generally described either in terms of symptomatic improvement or as pain scores, reducing the amount of information available for either outcome. We cannot be certain these outcomes were not collected across all studies but not reported if they failed to show statistical significance or consistent results. We performed a meta-analysis to get a pooled estimate of improvement rates, but may be criticized for doing so using such low quality data. Few studies sought pain data on individual pain symptoms, such as dyspareunia or pain on standing, preventing reflection on whether embolization reduces specific symptoms thought to be particularly indicative of pelvic vein congestion.

The pooled estimate of moderate to complete symptomatic improvement following embolization is consistent with previous limited reviews, as are the rates of coil

migration, although these too draw upon low quality case series. (31, 32) Technical success is high, although dependent on pelvic anatomy, and has been widely adopted around the world. Few studies addressed the impact on menstruation and fertility. This contrasts starkly with uterine artery embolization for the uterine fibroids, where there is considerable debate regarding the impact on ovarian function and pregnancy rates.(33, 34)

Whilst the data appears supportive, the quality of evidence is poor. Under the GRADE criteria, the methodological quality is very low and there is no direct comparative evidence against no embolization.(35) Some reflection on the only randomized controlled trial is warranted. The study population excluded those whose pain could be attributable to organic pathology or who responded to medroxyprogesterone, and who did not wish to retain their uterus and ovaries. The 118 patients were randomized to either embolization or hysterectomy with bilateral oophorectomy, plus hormone replacement therapy, or hysterectomy with unilateral oophorectomy, on the predominantly congested side.(14) The study reported that the embolization group and the hysterectomy with bilateral oophorectomy group had statistically significant improvement in pain reported on a visual analogues scale at 3, 6 and 12 months, whereas those with only unilateral oophorectomy did not, but these assertions have not be replicated. Furthermore, the method of randomization was unclear and there were substantial post-randomization exclusions, which undermine the credibility of the trial results.

We were unable to investigate heterogeneity of results across studies other than for the outcome of moderate to complete symptomatic improvement, reported in 6 studies, where moderate heterogeneity was identified. This could arise from the embolization technique, the way in which the question of improvement was presented and categorized or from the population included in the study.

The precision of the estimates for this outcome is moderate, due to the relatively small number of studies and participants per study, with a confidence interval of $\pm 10\%$ around the pooled rate of substantial symptomatic improvement of 75% in the short term. This would probably encompass a range of response rates that would be acceptable to women, given the low incidence of adverse events. However, we cannot be certain that

publication bias does not exist and that this results is not an overestimation of the true effect.

If we can accept that embolization provides pain relief, despite the limitations of the literature, the next questions are whether particular presenting characteristics can predict a successful outcome, and what the optimal technique is. A retrospective case series of 41 women access the relationship between technique (bilateral or unilateral), parity and location of varices (thigh or labial compared to pelvic) and clinical outcome. There was no statistically significant predictor of a successful outcome amongst these variables, although a trend towards a higher rate of success in grand multiparous women was noted. No association between these variables and treatment failure was observed, but in both circumstances, it may just be that there are too few women to observe a small association.(4)

No apparent trend for either metal coils or sclerosant has emerged. Stratification of the meta-analysis of symptomatic improvement by method is limited by the amount of data but seems to suggest the overall rate of substantial improvement is reflective of the studies using sclerosant at about 75%, whereas the two studies using solely coils had higher rates, at 89% and 100% respectively.(10, 11) No obvious differences between methods on the reduction in pain scores were seen. It may indeed be that the presentation of the varices and anatomy of the veins are the key determinants of successful elimination of reflux, with perhaps both methods being requiring for the most dilated veins.

Complications of embolization appear to be limited to short-term pain and fever in a reasonable proportion of sclerosant cases, or an uncommon incidence of coil migration. Coil placement is a relatively straightforward procedure but may be subject to recanalization or development of collaterals, as has been observed in male varicocele.(36) Some radiologists prefer liquid sclerosants the perception being that a more extensive embolus is produced, and also due to their cost compared with metal coils.(4)

Women should be counselled that the embolization, whilst apparently safe, may not provide complete relief of symptoms. There is scope for considerable further research

into the condition known as pelvic congestion syndrome, and in particular, an adequately powered randomized trial is essential to provide the necessary data on the effectiveness of embolization, but faces methodological challenges.

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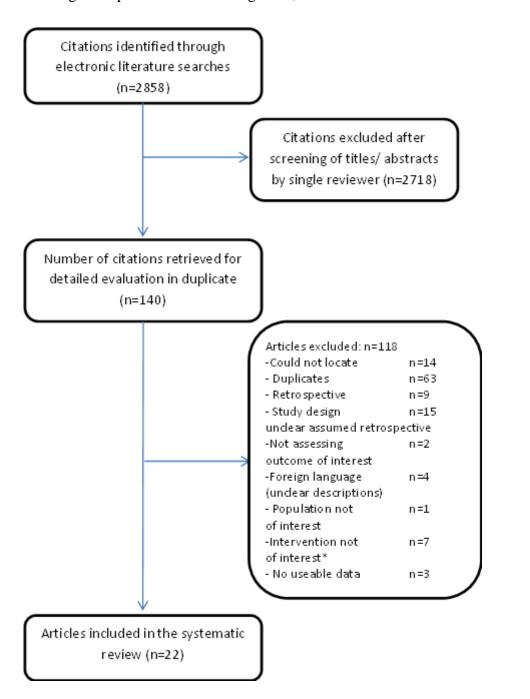


Figure 1: Flow diagram showing the study selection process for the systematic review of embolization and sclerotherapy for reducing chronic pelvic pain

Footnote:

* Seven studies of OV ligation were identified in an initial scoping search. We made a decision after registration on the PROSPERO database to exclude studies of ligation from this review, as it is rarely performed in current practice now that the technically less demanding and lower risk option of percutaneous vein embolization is widely available.

Table 1 Characteristics and key outcomes of studies selected for inclusion in systematic review of effectiveness of embolization of pelvic vein incompetence

Author,	Number	Treatment	Study type	Outcomes, follow up	Key results
date,				period	
country					
Capasso	19	OV vein glue,	Prospective	Subjective assessment	Early outcomes: 74% had improvements in pain
1997		coil or	observational	of pain relief within 4	symptoms (complete relief in 58%, partial in 16%).
Belgium		combined	study	weeks. Trans-abdominal	Improvement correlated with ultrasonographical
		embolization		Doppler ultrasound at 5	evidence of complete thrombosis of varices.
				weeks. Average 15	Dyspareunia (n=5) persisted. N=5 with persistent
				month follow up for	pain had re-intervention. 2 venous perforations that
				recurrence.	resolved.
Tarazov	6	OV coil	Not stated	Subjective reporting of	Complete alleviation of CPP in all women within 4
1997		embolization.		symptom Improvement,	weeks. Improved menstrual symptoms I 2 women
Russia				follow-up duration 1-4	with dysmenorrhea. No serious complications.

				years.	
Cordts	9	OV coil	Consecutive	Numerical rating scale	8 women (88.9%) had >80% immediate symptom
1998		embolization.	case series	of symptom relief, mean	relief. Two women had a mild or moderate return of
USA				follow-up 13 months	the symptoms at 6 and 22 months respectively. One
					lower lobe coil pulmonary embolus.
Scultetus	15	Sclerotherapy	Prospective	VAS of improvement.	12 had excellent improvement, 3 had moderate
2002	(treated	of varices	observation	Mean follow-up 2.3	improvement. No deep vein thrombosis reported.
USA	with	alone or with	study	years.	
	sclerothe	excision of			
	rapy)	varices.			
Venbrux	56	OV and	Prospective	VAS for pain, menstrual	Mean pain 7.8 at baseline decreased to 4.2 at 3-
2002		subsequent	observational	cycle questionnaire at 3,	months, 3.8 at 6 months, 2.7 at 12 months (p<0.001
USA		IIV coil	study	6 and 12 months post	for all comparisons). No significant changes in cycle
		embolization		procedure.	length.

Chung	106, of	OV or IIV coil	Randomized	VAS at 3, 6, and 12	Statistically significant decrease from baseline and
2003	whom	embolization,	control trial	months post-procedure,	between embolization and hysterectomy groups at all
South	52	Hysterectomy		patient global	time-points.
Korea	treated	with uni or		impression of change.	
	with	bilateral			
	emboliz	oophorectomy			
	ation				
Pieri	33	OV foam	Prospective	Subjective rating of	Improvement in pain in 61%. Mean OV diameter at
2003		sclerotherapy	observational	various pain symptoms	baseline right 4.5mm and left 6.3mm reduced to 3.10
Italy			study	at 1 month. Clinical	and 4.4mm respectively at follow-up. Seven patients
				assessment and mean	had transient flank pain.
				venous diameter by	
				ultrasound at 6 months.	
Kim	127	OV	Retrospectivel	Visual analogue scale	Mean pelvic pain at baseline 7.6 (SD 1.8) and 2.9

2006		coil/sclerosant	y identified	and composite clinical	(SD 2.8) (p < 0.0001) and 80% had significant
USA		embolization,	women	assessment at 3 and 6	improvement at mean 45 months follow-up. All pain
		+/- subsequent	followed-up	months and annually	symptoms significantly improved. Two coil
		IIV sclerosant	prospectively.	thereafter.	migrations.
		embolization			
Leal	239	Coil	Observational	Clinical assessment at 6	Complete resolution of pain symptoms in 120/ 239
Monedero		embolization	study	months post-procedure.	(50.2%) and partial relief in 95/239 (36.8%).
2006		+/- foam, of			Superficial phlebitis at point of venous access in 21
Spain		OV or IIV			women. No coil migrations.
Richardson	26	OV coil	Prospective	Visual analogue scale	No significant difference between groups in
2006		embolization,	case series,	for pain symptoms and	demographics and presenting symptoms. Coil group
Australia		+/- foam.	with historical	patient overall	pain score statistically significantly reduced from 6.6
			control group	satisfaction. Mean	(SD 1.9) to 4.0 (SD 2.8), from baseline. No
			undergoing	follow-up 22±13	statistically significant difference in pain reduction

			OV ligation.	months.	between ligation and embolization groups nor in
					overall satisfaction. No coil migration within 6
					weeks, one coil perforation detected at 5 months.
Creton	24	OV or IIV coil	Prospective	VAS for dysmenorrhea,	Statistically significant decreases in all three pain
2007		embolization	observational	dyspareunia and venous	symptoms and improvements in clinical assessment
France			study	pain (individually and	maintained. One coil migration.
				total); clinical	
				assessment at 45 days	
				and 1,2 and 3 years	
				follow up	
Greiner	13 (of	Coil or glue or	Observational	Repeat TVUS at 1 and 6	Complete resolution of symptoms in 10/13 and
2007	24	combined	study	months, 1 and 4 years.	significant improvement in 3/13. No recurrence of
France	emboliz	embolization	(assumed	Repeat clinical	PVI.
	ed)	of OV and	prospective)	assessment and	
		IIV.		venography at 4 years.	

Kwon	67	OV coil	Prospective	Categorical pain	82% reported total or significant pain reduction. Two
2007		embolization	study of	severity scale. Mean	coil migrations.
South			outcome with	follow up 45 months	
Korea			baseline pain		
			determined by		
			telephone		
			interview or		
			medical note		
			review		
Gandini	38	OV foam	Described as	VAS for 4 pain	Mean VAS for CPP showed decrease from 7.8 (SD
2008		sclerotherapy	retrospective	symptoms at 1, 3, 6 and	1.8) to 2.7(SD 2.8), from 4.9(SD 4.2) to 2.2(3.1) for
Italy			but included	12 months follow up	menstrual pain, from 3.3(SD 3.7) to 1.5(SD 2.7) for
			all patients at		dyspareunia and 3.5(SD 3.9) to 1.5(SD 3.0) for
			3 defined		urinary urgency at 12 months, all statistically
			time-points		significant.

Ratnam	218	Coil	Prospective	Repeat TVUS at 6-8	Of 193 with follow-up, 16 had residual mild reflux, 6
2008		embolization	inclusion,	weeks	had marked reflux and 3 had new reflux.
UK		of OV and IIV	retrospective		Two coil migrations, one misplacement, one case of
			data extraction		perineal thrombophlebitis.
			from medical		
			notes.		
Sukovatyk	59	Sclerotherapy	Not stated	Clinical examination,	Improvements (not defined) were classified as
h				USS and self-reported	excellent in 32.6%, good in 46.1%, satisfactory in
2008				quality of life	19.1% and unsatisfactory in 2.2% of the patients.
Russia					
Tropeano	20	Sclerotherapy	Prospective	VAS for pain, menstrual	Three women had repeat embolization after 3 months
2008		of the OV	observational	cycle questionnaire and	due to no change in symptoms and residual PVI on
Italy			study	ultrasound at 3, 6 and 12	ultrasound. 17 (85%) achieved marked to complete
				months post procedure.	relief until 6 months, with 2 describing a reduction in
					relief by 12 months,

					Median VAS pain scores decreased from at 8.0
					(range 6.0 to 10.0) at baseline to 2.0 (1.0 – 5.0), 2.5
					(1.5 - 5.0), and $3.0 (2.0 - 6.0)$ at 3, 6 and 12 months
					respectively, all statistical significantly reductions
					(p<.001).
Asciutto	35 (26	OV, IIV or	Prospective	VAS of pain at 1,2,3	VAS scores for isolated OVI: baseline mean 5.2 (SD
2009	also had	both with coil	observational	years of follow up	3.5) and 1.2 (SD 0.9) at 3 years; p<0.0001, non-
Germany	concurre	embolization	study		statistically significant reduction for combined OVI
	nt VV				and IIV or isolated IIV alone. At mean follow-up 45
	surgery)				months, overall 47% had sustained improvement. 3
					venous perforations that resolved.
D'Archam	193 (130	Coil	Prospective	Symptom rating on	11 (5.7%) were re-embolized between 3 months and
beau	had PVI)	embolization	observational	VAS before procedure	6 years. 91/102 (89.2%) patients with PCS symptoms
2010		of OV	study	and at 1 year.	reported improvement in symptoms on VAS.
Belgium					

Tinelli	28	OV foam	Not stated but	VAS for pain, clinical	At 1 month, 6 (21%) reported PVI symptoms, which
2012		sclerotherapy	follow-up at	examination and USS at	resolved by 6 months. Reduction in varicosity size
Italy			specific time-	10 days, 1 and 6 months	from 6.9mm (SD 2.1mm) on left and 5.1mm
			points.	post procedure.	(SD1.4mm) on right to <4.5mm in all embolized
					veins. 100% technical success with no adverse
					events beyond minor analgesics needs in 6 (21%)
					patients.
van der	21 who	Sclerotherapy	Prospective	5 point ordinal scale of	14 (66.7%) and 16 (76.2%) women had moderate or
Vleuten	responde	of OV.	observational	8 pain symptoms and	obvious improvement or no symptoms, at 2 months
2012	d		study	pelvic varices and	and cross sectional follow-up at mean 18 ± 122
Netherland	follow-			hemorrhoids, and global	months survey, respectively. All pain symptoms
S	up			impression of change.	except backache or urinary symptoms showed
	survey				statistically significant improvements. Nine (42.9%)
					women had a second embolization.
Meneses	10	Combined OV	Prospective	Venous clinical severity	Significant decrease in pain from 8.2 at baseline to

2013	and/or IIV	observational	score (VCSS) and VAS	4.0 at 3 months (p<0.001). Significant decrease in
Chile	embolization,	study	for pain at 3 months	VVCS from 8.4 at baseline to 3.6 at 3 months
	using		follow-up.	follow-up (P<0.001). No VV recurrence by 6
	sclerosant and			months.
	coil.			
	COII.			

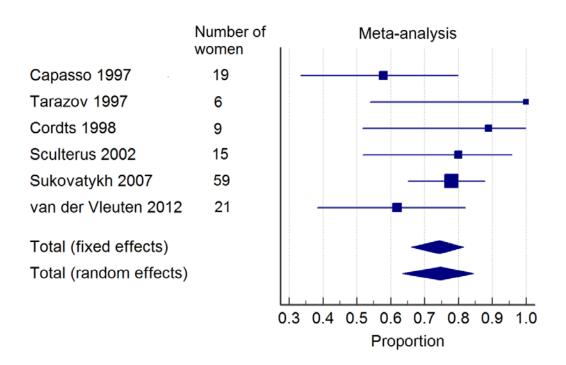


Figure 1 Meta-analysis of rates of complete, excellent or moderate (combined) improvement 4-8 weeks following embolization

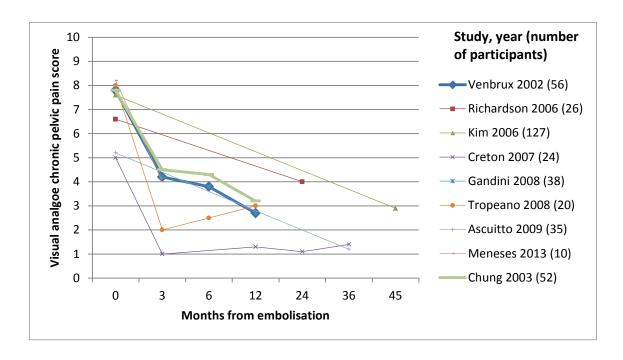


Figure 2 Time course of pain scores following embolization for pelvic vein incompetence

Table S1 Characteristics of studies selected for inclusion in systematic review of effectiveness of embolization of pelvic vein incompetence

Author, date,	Number	Patient group	Treatment	Study type	Outcomes,	Key results
country					follow up	
					period	
Capasso	19	Women with	OV vein glue	Prospective	Subjective	Early outcomes: 74%
1997		clinical and	(n=24), coil (n=2)	observational	assessment of	had improvements in
Belgium		ultrasonographic	or combined	study	pain relief	pain symptoms
		al or	(n=4)		within 4 weeks.	(complete relief in
		radiological	embolization; left		Trans-	58%, partial in 16%).
		evidence of PVI.	OV only n=13,		abdominal	Improvement
			bilateral n=6.		Doppler	correlated with
					ultrasound at 5	ultrasonographical
					weeks. Average	evidence of complete
					15 month follow	thrombosis of varices.

					up for	Dyspareunia (n=5)
					recurrence.	persisted. N=5 with
						persistent pain had re-
						intervention. 2 venous
						perforations that
						resolved.
Tarazov	6	Women with	Bilateral n=1 or	Not stated	Subjective	Complete alleviation
1997		clinical and	left unilateral n=5		reporting of	of CPP in all women
Russia		radiological	OV coil		symptom	within 4 weeks.
		evidence of PVI	embolization.		Improvement,	Improved menstrual
					follow-up	symptoms I 2 women
					duration 1-4	with dysmenorrhea.
					years.	No serious
						complications.
Cordts	9	Women with	Bilateral n=4 or	Consecutive	Numerical	8 women (88.9%) had

1998		clinical and	left unilateral n=4	case series	rating scale of	>80% immediate
USA		ultrasonographic	OV coil		symptom relief,	symptom relief. Two
		and/or	embolization.		mean follow-up	women had a mild or
		radiological			13 months	moderate return of the
		evidence of PVI.				symptoms at 6 and 22
						months respectively.
						One lower lobe coil
						pulmonary embolus.
Scultetus	15	Women with	Sclerotherapy of	Prospective	VAS of	12 had excellent
2002	(treated	"mild"	varices alone or	observation	improvement.	improvement, 3 had
USA	with	discomfort,	with excision of	study	Mean follow-up	moderate
	sclerothe	small varies and	varices.		2.3 years.	improvement. No deep
	rapy)	mild reflux by				vein thrombosis
		Doppler				reported.
		ultrasound.				

Venbrux	56	Women with	Bilateral OV	Prospective	VAS for pain,	Mean pain 7.8 at
2002		clinical and	(100%) and	observational	menstrual cycle	baseline decreased to
USA		ultrasonographic	subsequent IIV	study	questionnaire at	4.2 at 3-months, 3.8 at
		and/or	(77%) coil		3, 6 and 12	6 months, 2.7 at 12
		radiological	embolization		months post	months (p<0.001 for
		evidence of PVI.			procedure.	all comparisons). No
						significant changes in
						cycle length.
Chung	106, of	Pre-menopausal	a) OV or IIV coil	Randomized	VAS at 3, 6, and	Statistically significant
2003	whom 52	women with	embolization	control trial	12 months post-	decrease from baseline
South Korea	treated	idiopathic CPP	(n=52) b)		procedure,	and between
	with	and a score of	Hysterectomy		patient global	embolization and
	emboliza	≥5 on a	with bilateral		impression of	hysterectomy groups
	tion	modified	oophorectomy		change.	at all time-points.
		venography	(n=27) c)			

		scale, refractory	Hysterectomy			
		to MPA.	with unilateral			
			oophorectomy			
			(n=27)			
Pieri	33	Women with	OV foam	Prospective	Subjective	Improvement in pain
2003		clinical and	sclerotherapy	observational	rating of various	in 61%. Mean OV
Italy		ultrasonographic	(64% bilaterally)	study	pain symptoms	diameter at baseline
		al evidence of			at 1 month.	right 4.5mm and left
		PVI.			Clinical	6.3mm reduced to 3.10
					assessment and	and 4.4mm
					mean venous	respectively at follow-
					diameter by	up. Seven patients had
					ultrasound at 6	transient flank pain.
					months.	
Kim	127	Women with	Bilateral (85%) or	Retrospectivel	Visual analogue	Mean pelvic pain at

2006		clinical and	unilateral (15%)	y identified	scale and	baseline 7.6 (SD 1.8)
USA		radiological	OV	women	composite	and 2.9 (SD 2.8) (p <
		evidence of PVI,	coil/sclerosant	followed-up	clinical	0.0001) and 80% had
		including 25	embolization,	prospectively.	assessment at 3	significant
		with	with 85% having		and 6 months	improvement at mean
		hysterectomy.	subsequent IIV		and annually	45 months follow-up.
			sclerosant		thereafter.	All pain symptoms
			embolization			significantly
						improved. Two coil
						migrations.
Leal Monedero	239	Women with	Coil embolization	Observational	Clinical	Complete resolution of
2006		clinical and	with or without	study (unclear	assessment at 6	pain symptoms in 120/
Spain		radiological	foam, of OV or	whether	months post-	239 (50.2%) and
		evidence of PVI	IIV, with VV	prospective or	procedure.	partial relief in 95/239
		(with or without	surgery where	retrospective)		(36.8%). Superficial

		CPP) and lower	indicated s			phlebitis at point of
		limb VV				venous access in 21
						women. No coil
						migrations.
Richardson	26	Women with	Coil	Case series,	Visual analogue	No significant
2006		CPP and	embolization,	with historical	scale for pain	difference between
Australia		ultrasonographic	with or without	control group	symptoms and	groups in
		evidence of PVI.	foam, of OV.	undergoing	patient overall	demographics and
				OV ligation.	satisfaction.	presenting symptoms.
				Patient	Mean follow-up	Coil group pain score
				information	22±13 months.	statistically
				suggests		significantly reduced
				prospective.		from 6.6 (SD 1.9) to
						4.0 (SD 2.8), from

						baseline. No
						statistically significant
						difference in pain
						reduction between
						ligation and
						embolization groups
						nor in overall
						satisfaction. No coil
						migration within 6
						weeks, one coil
						perforation detected at
						5 months.
Creton	24	Pre-menopausal	OV or IIV coil	Prospective	VAS for	Statistically significant
2007		women with	embolization	observational	dysmenorrhea,	decreases in all three
France		dysmenorrhea/		study	dyspareunia and	pain symptoms and

		dyspareunia and			venous pain	improvements in
		radiological			(individually	clinical assessment
		evidence of PVI.			and total);	maintained. One coil
					clinical	migration.
					assessment at 45	
					days and 1,2 and	
					3 years follow	
					up	
Greiner	13 (of 24	Women with	Bilateral and	Observational	Repeat TVUS at	Complete resolution of
2007	embolize	clinical and	unilateral coil or	study	1 and 6 months,	symptoms in 10/13
France	d)	ultrasonographic	glue or combined	(assumed	1 and 4 years.	and significant
		al evidence of	embolization of	prospective)	Repeat clinical	improvement in 3/13.
		PVI with CPP	OV and IIV.		assessment and	No recurrence of PVI.
		and lower limb			venography at 4	
		VV.			years.	

Kwon	67	Women with	OV coil	Prospective	Categorical pain	82% reported total or
2007		clinical and	embolization	study of	severity scale.	significant pain
South Korea		radiological	(96% left OV	outcome with	Mean follow up	reduction. Two coil
		evidence of PVI	only)	baseline pain	45 months	migrations.
				determined by		
				telephone		
				interview or		
				medical note		
				review		
Gandini	38	Women with	Bilateral OV	Described as	VAS for 4 pain	Mean VAS for CPP
2008		CPP and	foam	retrospective	symptoms at 1,	showed decrease from
Italy		ultrasonographic	sclerotherapy (3%	but included	3, 6 and 12	7.8 (SD 1.8) to 2.7(SD
		evidence of PVI.	STSF)	all patients at 3	months follow	2.8), from 4.9(SD 4.2)
				defined time-	up	to 2.2(3.1) for
				points		menstrual pain, from

						3.3(SD 3.7) to 1.5(SD
						2.7) for dyspareunia
						and 3.5(SD 3.9) to
						1.5(SD 3.0) for urinary
						urgency at 12 months,
						all statistically
						significant.
Ratnam	218	Women with	Bilateral and	Prospective	Repeat TVUS at	Of 193 with follow-up,
2008		ultrasonographic	unilateral coil	inclusion,	6-8 weeks	16 had residual mild
UK		al evidence of	embolization of	retrospective		reflux, 6 had marked
		PVI and veins	OV and IIV, with	data extraction		reflux and 3 had new
		communicating	VV surgery	from medical		reflux.
		with lower limb	deferred to >8	notes.		Two coil migrations,
		VV	weeks post			one misplacement, one
			procedure.			case of perineal

						thrombophlebitis.
Sukovatykh	59	Women with	Sclerotherapy	Not stated	Clinical	Improvements (not
2008		clinical and			examination,	defined) were
Russia		ultrasonographic			USS and self-	classified as excellent
		and/or			reported quality	in 32.6%, good in
		radiological			of life	46.1%, satisfactory in
		evidence of PVI				19.1% and
						unsatisfactory in 2.2%
						of the patients.
Tropeano	20	Women with	Sclerotherapy of	Prospective	VAS for pain,	Three women had
2008		CPP and	the OV (15%	observational	menstrual cycle	repeat embolization
Italy		ultrasonographic	bilateral)	study	questionnaire	after 3 months due to
		evidence of PVI,			and ultrasound	no change in
		with no pelvic			at 3, 6 and 12	symptoms and residual
		pathology seen			months post	PVI on ultrasound. 17

	at laparoscopy		procedure.	(85%) achieved
	and			marked to complete
	embolization			relief until 6 months,
	possible			with 2 describing a
	anatomically.			reduction in relief by
				12 months,
				Median VAS pain
				scores decreased from
				at 8.0 (range 6.0 to
				10.0) at baseline to 2.0
				(1.0 – 5.0), 2.5 (1.5 -
				5.0), and 3.0 (2.0 –
				6.0) at 3, 6 and 12
				months respectively,
				all statistical

						significantly
						reductions (p<.001).
Asciutto	35 (26	Women with	OV (n=28),	Prospective	VAS of pain at	VAS scores for
2009	also had	clinical and	IIV(n=5) or both	observational	1,2,3 years of	isolated OVI: baseline
Germany	concurre	radiological	(n=2) with coil	study	follow up	mean 5.2 (SD 3.5) and
	nt VV	evidence of PVI.	embolization			1.2 (SD 0.9) at 3
	surgery)					years; p<0.0001, non-
						statistically significant
						reduction for
						combined OVI and
						IIV or isolated IIV
						alone. At mean follow-
						up 45 months, overall
						47% had sustained
						improvement. 3

						venous perforations
						that resolved.
D'Archambeau	193 (130	Women with	Bilateral (4.7%)	Prospective	Symptom rating	11 (5.7%) were re-
2010	had PVI)	clinical and	or unilateral coil	observational	on VAS before	embolized between 3
Belgium		radiological	(94.3% left, 1%	study	procedure and at	months and 6 years.
		evidence of PVI.	right) coil		1 year.	91/102 (89.2%)
			embolization of			patients with PCS
			OV			symptoms reported
						improvement in
						symptoms on VAS.
Tinelli	28	Women with	OV foam	Not stated but	VAS for pain,	At 1 month, 6 (21%)
2012		ultrasonographic	sclerotherapy	follow-up at	clinical	reported PVI
Italy		and radiological	(29% bilaterally)	specific time-	examination and	symptoms, which
		evidence of PVI		points.	USS at 10 days,	resolved by 6 months.
					1 and 6 months	Reduction in

					post procedure.	varicosity size from
						6.9mm (SD 2.1mm)
						on left and 5.1mm
						(SD1.4mm) on right to
						<4.5mm in all
						embolized veins.
						100% technical
						success with no
						adverse events beyond
						minor analgesics needs
						in 6 (21%) patients.
van der Vleuten	21 who	Women with	Bilateral or	Prospective	5 point ordinal	14 (66.7%) and 16
2012	responde	CPP and	unilateral	observation	scale of 8 pain	(76.2%) women had
Netherlands	d follow-	radiological	sclerotherapy of	study for 2	symptoms and	moderate or obvious
	up	evidence of PVI	OV.	month follow-	pelvic varices	improvement or no

	survey	with or without		up, with cross	and	symptoms, at 2 months
		lower limb VV		sectional	hemorrhoids,	and at the survey,
				follow-up at	and global	respectively. All pain
				mean 18 ±122	impression of	symptoms except
				months	change.	backache or urinary
						symptoms showed
						statistically significant
						improvements. Nine
						(42.9%) women had a
						second embolization.
Meneses	10	Women	Combined OV	Prospective	Venous clinical	Significant decrease in
2013		undergoing	and/or IIV	observational	severity score	pain from 8.2 at
Chile		repeat surgery	embolization,	study	(VCSS) and	baseline to 4.0 at 3
		for VV	using sodium		VAS for pain at	months (p<0.001).
		recurrence and	morrhuate		3 months	Significant decrease in

baseline to 3.6 at 3
months follow-up
(P<0.001). No VV
recurrence by 6
months.

Table S2a. Demographics details of the patients in the included studies of effectiveness of embolization (age)

Range 24-59
24-59
25-40
23 10
20-43
20 13
24-48
21 10
16-66
10 00
36-56

Creton 41.5 31-50 2007 41 32-65 Greiner 41 32-65 2007 39.1 9 25-64 Gandini 36.9 22-44 2008 46.3 28-70 Sukovatykh NS 2008 Tropeano 36 19-50 2008 49 11 27-72 D'Archambeau 40.3 20-66 Tinelli 51 43-59 van der Vleuten 41.7 9.6 30-71 Meneses 38 25-39	2006*			
2007 Greiner 2007 41 32-65 Kwon 2007 39.1 9 25-64 Gandini 2008 Ratnam ** 2008 Sukovatykh 2008 Tropeano 2008 Asciutto 2009 D'Archambeau 2010 Tinelli 2012 41.7 9.6 32-65 32-65 32-65 32-64 32-64 32-64 36-9 22-44 28-70	Creton			
Mathematical Exercises Mathematical Exerci	2007	41.5		31-50
2007 39.1 9 25-64 2007 39.1 9 25-64 2007 36.9 22-44 2008 46.3 28-70 Sukovatykh NS 2008 Tropeano 36 19-50 2008 49 11 27-72 2009 49 11 27-72 D'Archambeau 40.3 20-66 2010 51 43-59 van der Vleuten 41.7 9.6 30-71	Greiner	<i>A</i> 1		22, 65
39.1 9 25-64 Gandini 36.9 22-44 Ratnam # 2008 Sukovatykh NS 2008 Tropeano 2008 Asciutto 2009 D'Archambeau 2010 Tinelli 2012 van der Vleuten 2012	2007	41		32-03
2007 Gandini 2008 Ratnam # 2008 Sukovatykh 2008 Tropeano 2008 Asciutto 2009 D'Archambeau 2010 Tinelli 2012 Van der Vleuten 2012 41.7 9.6 36.9 22-44 28-70 28-70 2008 36 11 27-72 2009 2010 30-71	Kwon	39.1	Q	25-64
2008 Ratnam # 2008 Sukovatykh 2008 Tropeano 2008 Asciutto 2009 D'Archambeau 2010 Tinelli 2012 Van der Vleuten 2012 36.9 22-44 28-70 28-70 28-70 28-70 29-70 29-70 29-70 29-70 20-70 20-70 20-70 40.3 20-66 20-71 41.7 9.6 30-71	2007	37.1	,	23-04
2008 Ratnam # 2008 Sukovatykh 2008 Tropeano 2008 Asciutto 2009 D'Archambeau 2010 Tinelli 2012 Van der Vleuten 2012 46.3 28-70 28-70 28-70 28-70 28-70 28-70 29-60 19-50 29-60 11 27-72 20-66 20-66 30-71	Gandini	36.9		22-44
2008 Sukovatykh 2008 Tropeano 2008 Asciutto 2009 D'Archambeau 2010 Tinelli 2012 Van der Vleuten 2012 28-70 28-70 28-70 28-70 28-70 28-70 28-70 28-70 28-70 29-50 49 11 27-72 20-66 20-66 49 40.3 20-66 43-59 30-71	2008	30.7		22-44
2008 Sukovatykh 2008 Tropeano 2008 Asciutto 2009 D'Archambeau 2010 Tinelli 2012 van der Vleuten 2012 36 19-50 27-72 2009 11 27-72 20-66 20-66 30-71	Ratnam #	46.3		28-70
Tropeano 2008 Tropeano 36 19-50 Asciutto 2009 D'Archambeau 2010 Tinelli 2012 41.7 9.6 36 19-50 27-72 20-66 27-72 49 40.3 20-66 30-71	2008	40.3		20-70
2008 Tropeano 2008 Asciutto 2009 D'Archambeau 2010 Tinelli 2012 41.7 9.6 19-50 19-50 27-72 27-72 20-66 20-66 49 11 27-72 20-66 30-71	Sukovatykh	NS		
Asciutto 49 11 27-72 2009 D'Archambeau 2010 Tinelli 51 2012 41.7 9.6 19-50 19-50 19-50 19-50 19-50 19-50 49 27-72 20-66 20-66 30-71	2008	113		
Asciutto 49 11 27-72 2009 D'Archambeau 20-66 2010 Tinelli 2012 41.7 9.6 30-71	Tropeano	36		19-50
2009 D'Archambeau 40.3 20-66 Tinelli 2012 41.7 9.6 30-71	2008	30		17 30
2009 40.3 20-66 D'Archambeau 40.3 20-66 Tinelli 51 43-59 van der Vleuten 41.7 9.6 30-71 2012 30-71 30-71	Asciutto	49	11	27-72
2010 Tinelli 51 2012 van der Vleuten 2012 41.7 9.6 30-71	2009	77		27 72
2010 Tinelli 2012 van der Vleuten 2012 43-59 43-59 41.7 9.6 30-71	D'Archambeau	40.3		20-66
2012 51 43-59 van der Vleuten 41.7 9.6 30-71	2010	10.5		20 00
2012 van der Vleuten 41.7 9.6 30-71	Tinelli	51		43-59
2012 41.7 9.6 30-71	2012	<i>3</i> 1		TJ*J/
2012	van der Vleuten	Δ1 7	9.6	30-71
Meneses 38 25-39	2012	41./	7.0	30 - 71
	Meneses	38		25-39

2013		

^{*} Data for whole reported population, not solely those undergoing embolization

[#] Data recorded only for first 60 patients of 218 in study

[&] Described as mean parity and gravida in 15 parous women of the 19 in study

Table S2b. Demographics details of the patients in the included studies of effectiveness of embolization (parity)

Author		Parity											
(date)		(Gı	ravida)										
	Mean	SD	Range	% Nulliparous									
Capasso 1997	2 (2)&		0(0) to 5(6)	22.2									
Tarazov 1997	1.2 (6.5)		0(4) to 2(9)	16.6									
Cordts 1998	>2 (>2)			0									
Scultetus 2002 ^{£*}	3.1		2 to 5										
Venbrux 2002	NS												
Chung 2003	2.1	1.1		7.7									
Pieri 2003	NS												
Kim 2006	NS												

Leal Monedero	NS			
2006				
Richardson	3.3	1.2		
2006*				
Creton	NS (2.5)		(1 to 4)	
2007				
Greiner	4		2(2) to 8(8)	0
2007				
Kwon	2.4			0
2007	2. 4			O
Gandini				13.1
2008				13.1
Ratnam #				3.3
2008				3.3
Sukovatykh	NS			
2008	No			
Tropeano	0.9(0.9)	0.9	0 to 2	46
2008	0.9(0.9)	0.7	0 to 2	40
Asciutto	NS(2.5)		0 to 7	
2009	110(2.3)		0 10 7	
D'Archambeau	NS			
2010	. IND			
Tinelli	2.1			
2012	2.1			

van der Vleuten	• 0			
2012	2.9	1.1	2 to 6	
) /				
Meneses	3.5		2 to 5	
2013	3.3		2 10 3	
2010				

^{*} Data for whole reported population, not solely those undergoing embolization

[#] Data recorded only for first 60 patients of 218 in study

[&]amp; Described as mean parity and gravida in 15 parous women of the 19 in study

Table S3 Quality assessment of case series included in the systematic review of effectiveness of embolization for pelvic congestion syndrome

Study	Ai	Prospe	Mu	Eligib	Compa	Techn	Other	Outc	Vali	Stati	Timep	Los	Varia	Adv	Conclu	Conf
	m	ctive	lti-	ility	rable	ique	interve	omes	d	stics	oints	s to	bility	erse	sions	licts
			cen		pain at		ntions	descri	outc			foll		even		
			ter		baselin			bed	ome			ow-		ts		
					e							up				
Capasso	Y	U	N	N	U	Y	Y	N	N	N/A	N	U	N/A	Y	Y	N
1997																
Tarazov	Y	U	N	N	Y	Y	N	N	N	N/A	Y	U	N/A	Y	Y	N
1997																
Cordts	Y	Y	N	N	Y	Y	Y	U	U	N/A	N	U	N/A	Y	Y	N
1998																
Scultetus	Y	U	U	N	Y	Y	U	Y	U	N	N	Y	N/A	Y	U	N
2002																
Venbrux	Y	Y	U	N	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N

2002																
Pieri	Y	U	N	N	U	Y	Y	N	N	N	Y	U	N/A	Y	U	N
2003																
Kim	Y	Y	N	N	U	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	None
2006																
Leal	Y	U	N	Y	U	Y	Y	N	N	N	N	U	N/A	N	Y	N
Moneder																
o 2006																
Richards	Y	Y	N	N	U	Y	U	Y	Y	Y	N	U	Y	Y	Y	N
on 2006																
Creton	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	N/A	Y	Y	N
2007																
Greiner	Y	Y	N	N	U	Y	Y	Y	Y	N/A	Y	Y	N	Y	Y	N
2007																
Kwon	Y	U	N	N	N	Y	Y	Y	Y	N/A	Y	Y	N	Y	Y	N
2007																

Gandini	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	N
2008																
Ratnam	Y	Y	N	N	U	Y	Y	N	N	N	Y	Y	N/A	Y	Y	N
2008																
Tropean	Y	Y	N	N	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
o 2008																
Asciutto	Y	Y	N	Y	U	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	None
2009																
D'Archa	Y	Y	U	U	U	Y	U	Y	Y	U	Y	Y	N/A	N	Y	N
mbeau																
2010																
Tinelli	Y	U	Y	Y	Y	Y	Y	Y	U	U	Y	U	Y	Y	Y	N
2012																
Van der	Y	Y	N	N	U	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	None
Vleurten																
2012																

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Meneses	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	U	Y	Y	Y	N
2013																

Table S4 Pain scores before and after embolization of pelvic vein incompetence

	Time-p	oint (mont	ths)				
Study	0	3	6	12	24	36	45
Venbrux 2002	7.8	4.2 ^b	3.8 b	2.7 b			
Chung	7.8	4.5	4.3(0.8)	3.2 (0.9)			
2003	(1.2)	$(0.9)^{a}$	a	a			
Kim	7.6						2.9
2006	(1.8)						$(2.8)^{d}$
Richardson	6.6				4.0		
2006	(1.9)				$(2.8)^{c}$		
Creton							
2007	5	1.0°		1.3 °	1.1 °	1.4 ^c	
	7.8	4.2	3.8	2.7			
Gandini 2008	(1.8)	(1.9) ^a	$(0.9)^{a}$	$(2.8)^{a}$			
Tropeano 2008	8* ^b	2* b	2.5* b	3* b			
	5.2					1.2	
Asciutto 2009	(3.5)			2.1	1.5	$(0.9)^{d}$	
	8.2	4.0					
Meneses 2013	(0.9)	(1.7) ^c					

Key: *median

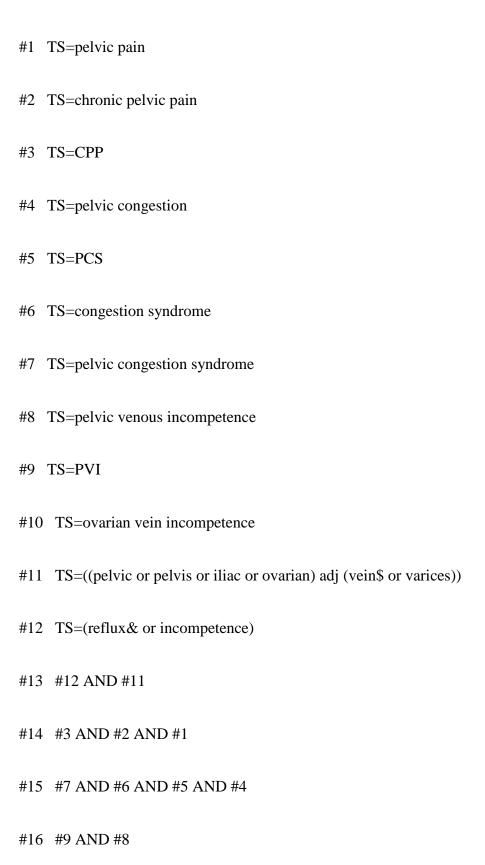
P values: a<0.05; b<0.01, c<0.001, d<0.0001, compared to baseline, as reported.

 $Supplementary\ appendix-Search\ strategies$

Search strategy for population and treatment

All databases searched from inception to November 2013.

BIOSIS WEB OF KNOWLEDGE:



#17	#16 OR #15 OR #14 OR #13 OR #10
#18	TS=treatment
#19	TS=therap\$
#20	TS=emboli*ation
#21	TS=sclerotherapy
#22	TS=sc*lerotherapy
#23	TS=ligation
#24	TS= interventional radiology
#25	TS=therapeutic emboli*ation
#26	TS=balloon occlusion
#27	TS=occulsion
#28	TS=dilatation
#29	TS=vasculari*ation
#30	TS=endovascular surgery
#31	TS=laparoscopic surgery
#32	TS=vascular surgical procedure
#33	TS=vascular surgery

#34 TS=embolotherapy

#35 #34 OR #33 OR #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR #24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18

#36 #35 AND #17

BRITISH NURSING INDEX:

Searched for: all (pelvic congestion)

CINAHL:

- S1 TX=pelvic congestion
- S2 TX=PCS
- S3 TX=congestion syndrome
- S4 TX=pelvic congestion syndrome
- S5 TX=S1 OR S2 OR S3 OR S4
- S6 TX=treatment
- S7 TX=therapy
- S8 TX=emboli*ation
- S9 TX=embolisation
- S10 TX=embolization

S11 TX=sclerotherapy
S12 TX=sc*lerotherapy
S13 TX=ligation
S14 TX=balloon occlusion
S15 TX=occlusion
S16 TX=dilatation
S17 TX=vasculari*ation
S18 TX=endovascular surgery
S19 TX=laparoscopic surgery
S20 TX=embolotherapy
S21 S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
OR S17 OR S18 OR S19 OR S20
S22 S5 AND S21
COCHRANE LIBRARY:
Pelvic congestion AND PCS search – HTAs
Pelvic congestion AND PCS search – trials

refl	ux AND vein search - Cochrane reviews
refl	ux AND vein search – HTAs
refl	ux AND vein search - Other reviews
refl	ux AND vein search – trials
DA	RE: pelvic congestion
	reflux AND vein
EM	IBASE: <1980 to 2013 Week 14>
1	exp Pelvic pain/ or chronic pelvic pain.mp.
2	CPP.mp.
3	pelvic congestion.mp.
4	PCS.mp.
5	congestion syndrome.mp.
6	pelvic congestion syndrome.mp.
7	pelvic venous incompetence.mp.
8	PVI.mp.
9	ovarian vein incompetence.mp.

10	((pelvic or pelvis or iliac or ovarian) adj (vein\$ or varices)).mp.
11	(reflux\$ or incompetence).mp.
12	10 and 11
13	1 and 2
14	3 and 4
15	3 and 4 and 5 and 6
16	7 and 8
17	9 or 12 or 13 or 15 or 16
18	treatment.mp.
19	therap\$.mp.
20	emboli*ation.mp.
21	exp Sclerotherapy/ or sc*lerotherapy.mp.
22	ligation.mp. or exp ligation/
23	interventional radiology.mp. or exp Radiology, Interventional/
24	exp Embolization, therapeutic/ or balloon occulsion.mp.
25	occulsion.mp.
26	dilatation.mp. or exp Dilatation/
27	vasculari*ation.mp.

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28	endovascular surgery.mp.
29	laparoscopic surgery.mp.
30	exp VascularSurgical Procedures/ or vascular surgery.mp.
31	embolotherapy.mp. or exp Embolization, therapeutic/
32	18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33	17 and 32
IME	MR: pelvic congestion
	reflux vein
IMS	EAR: pelvic congestion syndrome
IND	EX OF SCIENTIFIC AND TECHNICAL PROCEEDINGS:
Pelvi	c congestion syndrome AND vein

LILACS: pelvic AND congestion

reflux AND vein

MEDION: pelvic AND congestion

14 3 and 4

reflux AND vein

ME	EDLINE: Ovid MEDLINE(R) < 1946 to March Week 1 2013>
1	exp Pelvic Pain/ or chronic pelvic pain.mp.
2	CPP.mp.
3	pelvic congestion.mp.
4	PCS.mp.
5	congestion syndrome.mp.
6	pelvic congestion syndrome.mp.
7	pelvic venous incompetence.mp.
8	PVI.mp.
9	ovarian vein incompetence.mp.
10	((pelvic or pelvis or iliac or ovarian) adj (vein\$ or varices)).mp.
11	(reflux\$ or incompetence).mp.
12	10 and 11
13	1 and 2



PAHO: pelvic AND congestion

pelvic AND congestion AND syndrome

reflux AND vein

POPLINE: pelvic congestion syndrome

pelvic congestion

reflux vein

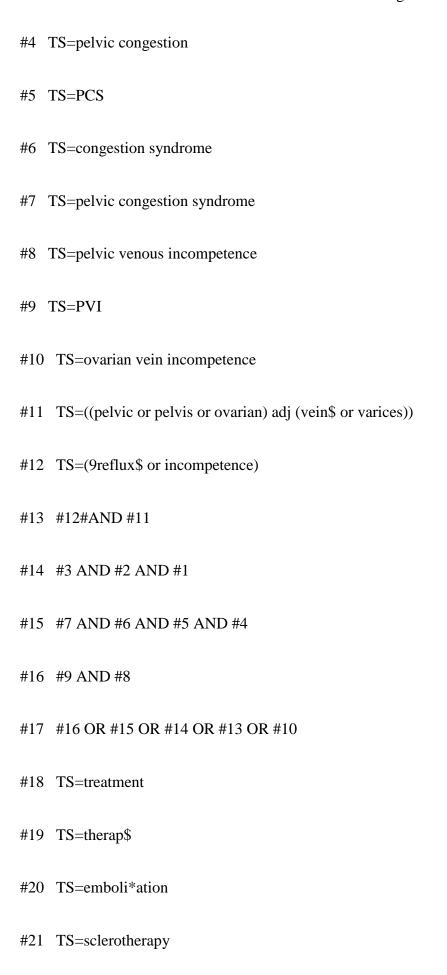
SciELO: pelvic AND congestion AND syndrome

reflux AND vein

pelvic congestion

WEB OF SCIENCE:

- #1 TS=pelvic pain
- #2 TS=chronic pelvic pain
- #3 TS=CPP



#22	TS=sc*lerotherapy
#23	TS=ligation
#24	TS=interventional radiology
#25	TS=therapeutic emboli*ation
#26	TS=balloon occlusion
#27	TS=occlusion
#28	TS=dilatation
#29	TS=vasculari*ation
#30	TS=endovascular surgery
#31	TS=laparoscopic surgery
#32	TS=vascular surgical procedure
#33	TS=vascular surgery
#34	TS=embolotherapy
#35	#34 OR #33 OR #32 OR #31 OR #30 OR #29 OR #28 OR #27 OR #26 OR #25 OR
	#24 OR #23 OR #22 OR #21 OR #20 OR #19 OR #18
#36	#35 AND #17

WPRIM: pelvic congestion

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reflux vein