The relationship between pelvic vein incompetence and chronic pelvic pain in women: systematic reviews of diagnosis and treatment effectiveness

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Scientific summary

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Background

Pelvic congestion syndrome (PCS) is described as chronic pelvic pain (CPP) 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 CPP. PCS is predominantly observed in multiparous women of reproductive age, suggesting both a mechanical and a hormonal mechanism.

Diagnostic methods

The identification of incompetent pelvic veins is essential for the diagnosis of PCS. Non-invasive methods such as ultrasound and magnetic resonance imaging are inevitably the first line of investigation, with assessment of the blood velocity and flow pattern a crucial part of any assessment of PVI. The accuracy of these techniques for establishing PVI, compared with the gold standard of direct visualisation through selective venography, is unclear.

Treatment

Elimination of the blood flow through an incompetent vein is a recognised strategy for reducing the impact of symptoms. This can be achieved via percutaneous introduction of an embolic agent, such as a metal coil or a sclerosant, upstream of the dilated or refluxing veins. Once the incompetent vein is occluded, blood is diverted via other veins, and, in time, new vessels form in the place of the original. Pelvic vein embolisation is now widely used, and has become the principal treatment for PCS, with high success rates often cited. However, robust data on its effectiveness are lacking.

Objectives

The commissioning brief asked two questions:

1. What is the relationship between refluxing pelvic veins and pelvic pain syndromes?
2. What is the evidence that the embolisation of refluxing veins is effective in pelvic pain syndromes?

To address these questions, our proposal had the following objectives:

- To assess the terminology, definitions and criteria used in the description and diagnosis of PCS.
- To systematically and critically review the evidence regarding the association between radiological observations of incompetent pelvic veins and the symptoms of CPP.
- To estimate the diagnostic accuracy of various non-invasive imaging techniques, compared with venography, in a systematic review.
- To conduct a systematic review of the clinical effectiveness of embolisation of incompetent pelvic veins.
- To collect individual patient data (IPD) from available studies involving embolisation in order to identify factors associated with successful outcome, and perform IPD meta-analysis if possible.
• To survey the clinical practice of UK and international pain specialists and interventional radiologists with respect to the diagnosis and management of PCS, including the latter group’s prior beliefs of the effectiveness of embolisation for PCS.
• To survey members of a pelvic pain support group to assess the lay awareness and understanding of PCS.
• To elicit an opinion from interventional radiologists and support group members on the desirability of a randomised controlled trial of pelvic vein embolisation.

**Methods**

For the systematic reviews of accuracy and effectiveness, a comprehensive search strategy was developed, and applied to databases from inception to March 2014 and September 2013, respectively. This was used in the 17 bibliographic databases including Cumulative Index to Nursing and Allied Health Literature, The Cochrane Library, Database of Abstracts of Reviews of Effects, EMBASE, Medion, MEDLINE and Web of Science. Bibliographies of all relevant primary articles and reviews were hand-searched and no language restrictions were applied during the searching phase.

Search terms for the condition included ‘pelvic pain’, ‘pelvic congestion’, ‘pelvic or ovarian vein’, ‘incompetence’ and ‘reflux’; for the intervention the terms included ‘treatment’, ‘endovascular therapy’, ‘interventional radiology’, ‘embolisation’, ‘sclerotherapy’, ‘ligation’ and ‘occlusion’ and for imaging tests the terms included ‘ultrasound’, ‘magnetic resonance imaging’, ‘computed tomography’, ‘angiography’, ‘phlebography’ and ‘venography’. There was no restriction on study design in either search. Identification of relevant citations for the reviews of diagnostic definitions and association used the studies identified by these searches.

All manuscripts selected for inclusion were assessed for their methodological quality using the Newcastle–Ottawa Scale for the association review, the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) scale for the accuracy review and a checklist for case series, and Cochrane Risk of Bias tool for the effectiveness review.

The quality and heterogeneity generally precluded meta-analysis and so results were tabulated and described narratively. We considered that the proposed IPD meta-analysis would not yield enough comparable, high-quality data to make any sophisticated analysis worthwhile and so we did not proceed with this.

The three surveys used SurveyMonkey™ (www.surveymonkey.com; Palo Alto, CA, USA) as the platform and were provided to pain specialists attending a conference, members of the British Society of Interventional Radiology and the membership of the Pelvic Pain Support Network.

**Results**

**Studies included in the four reviews**

We identified six relevant association studies, all which had issues regarding the selection of the controls or the size of the study. In the accuracy review, 10 studies involving ultrasound and two studies of magnetic resonance venography, all compared against conventional venography, were included. Over half had issues such as partial verification bias, precluding the calculation of accuracy parameters. The effectiveness review comprised 21 case series and one poor-quality randomised trial reporting on 1308 women. We attempted to restrict the review to prospective studies in order to reduce selection bias, but in some studies it was impossible to be completely certain from the methodology that included participants were not retrospectively identified from medical records. The studies included in the accuracy and effectiveness reviews were also considered for the assessment of definitions of PCS.
**Review results**

There was no single, clearly defined criterion for a diagnosis that was reported in the all of studies included in the review. The majority cited pelvic pain, dilated ovarian veins and venous reflux or congestion as principal features of PCS, but many did not give thresholds or further clarification, or, where they did, these were heterogeneous.

In six case–control studies, five had useable data from women with and without CPP, where we found that the associations were generally fairly similar, with three studies showing statistically significant associations (odds ratios of between 31 and 117). The two smallest studies failed to reach statistical significance in the odds of association, perhaps because they were too small to detect a difference. The proportion of women found to have PVI who reported CPP ranged considerably, from 39% to 91%. Polycystic ovaries were observed more frequently in the group with CPP and PVI in two studies. The prevalence of PVI ranged widely, although the majority of women with PVI had CPP. Conversely, in the four studies of asymptomatic women undergoing pelvic vein imaging for other reasons, no more than half had PVI, although again the prevalence ranged widely. Where lower-limb venous insufficiency was seen, between 60% and 77% of women also had pelvic varices.

Transvagal ultrasound (TVUS) with Doppler has a place in the screening of women for pelvic varices, although the data on its accuracy are limited. One study provided diagnostic accuracy parameters of 96% sensitivity [95% confidence interval (CI) 92% to 99%] and 100% specificity (lower 95% CI 97%), with positive and negative predictive values of 100% and 94%, respectively. Similarly, magnetic resonance venography appears to be reproducible, but accuracy data are limited to one study that suggested 88% sensitivity and 67% specificity for identifying PVI in the OV. Imaging modalities that demonstrate both venous dilatation and reflux are necessary.

In the systematic review of embolisation for PVI, approximately one-third of patients clearly had bilateral embolisation, with metal coil placement being the dominant technique. Early substantial relief from pain symptoms was observed in approximately 75% of women, a figure 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. Reintervention rates were generally low. Where measured, embolisation reduced the diameter of dilated veins to a significant degree, with minimal residual reflux. There were few data on the impact on menstruation, ovarian reserve or fertility, but no concerns were noted. Transient pain was a common occurrence following foam embolisation, while there was a < 2% risk of coil migration.

**Survey results**

From the three surveys, a few key themes were identified, perhaps most significantly that there are some dissenting opinions regarding PCS as a cause of CPP. First of all, although pain specialists and interventional radiologists vary in their approach to diagnosis, it is obvious that surgical management does not appear to be favoured. The majority of interventional radiologists do not perform many, if any, embolisations for PVI, and although their confidence in the procedure is reasonably high, they have a desire to see the evidence base strengthened. Even among women with CPP, fewer than half had any knowledge about PCS.

**Conclusions**

The data supporting the diagnosis and treatment of PVI in the presence of CPP are limited and of variable quality, and considerable further high-quality research is required to thoroughly address the research question. There is some evidence to tentatively support several of the required criteria which would indicate a causative association, but it cannot be stated that PVI is the cause of CPP in women who have no other pathology, a conclusion echoed in some dissenting views among the clinical community. Transvagal Doppler ultrasound and magnetic resonance venography are widely used and useful screening methods, but, ultimately, they cannot replace conventional venography if embolisation is planned. Embolisation appears to provide good to complete symptomatic relief in the majority of women.
**Implications for health care**

There exists a proportion of women for whom no cause for their pain can be found at laparoscopy; this causes anxiety for the patient, and the search for a diagnosis can be protracted, placing a significant demand on health-care resources. The strength of the evidence with respect to diagnosis and management is insufficient for any clinical recommendations to be made, but some good practice points can be listed. When taking a clinical history from a woman with CPP, gynaecologists should ask about specific pain symptoms, including whether pain is more severe after periods of standing and relieved by lying down. If this identifies incompetent pelvic veins, the radiologist can discuss the possibility of PCS as a diagnosis with her gynaecologist, highlighting the uncertainty in the data. In examining the patient, the presence of any vulval and lower-limb varicose veins should be noted. Transvaginal Doppler ultrasound should be available for women exhibiting symptoms indicative of PVI. If this identifies incompetent pelvic veins, the possibility of PCS as a diagnosis can be discussed with the patient’s gynaecologist, highlighting the uncertainty in the data. If there are interventional radiologists available who perform embolisation of pelvic veins, a referral may be considered. Women should be counselled that the embolisation, although apparently safe, may not provide complete relief of symptoms.

**Recommendations for research**

There is scope for considerable further research, with robust methodology and of adequate size. The question of the association of PVI and CPP requires a well-powered case–control study, in which women with CPP would be matched to two or more pain-free controls, using age and/or parity to match. All women would need to provide a standardised account of their pain symptoms, their gynaecological and obstetric history, and be examined for vulval or lower-limb varicose veins, before undergoing a consistent TVUS assessment using the most modern Doppler technology. Interpretation of the ultrasound and Doppler data should be undertaken in duplicate, with readers blind to each other’s assessment, to determine interobserver reliability. Ideally, a small subsample of patients should have the same ultrasound procedure performed at two time points in order to assess if timing in relation to the menstrual cycle is important, and to assess intraobserver consistency. This would provide data on the odds of PVI being associated with CPP and the reproducibility of ultrasound protocol.

This potential association study is predicated on there being a clear definition of PVI, but it will also provide data to derive the diagnostic performance of each individual criterion, in terms of the ability to discriminate PCS from pain-free controls. The potential criteria themselves should be identified by consensus among women with CPP and clinical researchers in the field. For example, if ovarian vein dilatation is considered an important observation for a diagnosis of PVI, a receiver operating curve could be produced, using various thresholds to define dilatation, and the optimum cut-off value could be obtained. Those parameters with a statistically significant difference between the CPP and pain-free groups of women would be incorporated into a logistic regression model. The regression coefficients of the best-fit model could be used to weight scores for each criterion before summation to a combined score.

A further study of women with and without CPP who were prepared to have TVUS with Doppler and conventional venography would be required to provide the threshold for the total score, in addition to reliably determining the accuracy of TVUS with Doppler, again mapping the score on a receiver operating curve to determine the cut-off value that provides the optimum clinical performance with respect to sensitivity and specificity. Finally, the scoring system would be validated in a prospective study of women with CPP to determine its accuracy. This would then provide a practical, valid tool for clinical use that would assist in the identification of women for invasive confirmatory venography and, potentially, treatment of PCS.

Assuming that a clear diagnostic standard for PCS can be obtained in this method, the issue remains of whether or not embolisation is an effective treatment. An adequately powered randomised trial is essential to provide the necessary data, but this faces methodological challenges. Pain is a subjective phenomenon and prone to measurement bias unless a placebo or sham intervention is provided. A conventional venogram would be required to verify PVI immediately prior to randomisation between a legitimate or
sham embolisation. It would be challenging to maintain the blinding of the patient during the procedure, as she would merely be under sedation, but ethical, given the necessity of blinding in reducing the risk of bias and the fact that there is a low risk of complications from venography.

Finally, an economic evaluation of the diagnostic pathway and of embolisation will provide the final evidence on whether or not the proposed management strategy is cost-effective. It would be of general benefit in the area of CPP to collect information on overall and condition-specific quality of life and on the quantity and type of health-care resources consumed by women, as there is little contemporary evidence in this field.

Study registration

This study is registered as PROSPERO CRD42012002237 and CRD42012002238.

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