The Efficacy Of Platelet-Rich Plasma In Pelvic Floor Reconstruction Surgery: A Scoping Review Of Literature

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Abstract

Objective: Platelet-rich plasma (PRP) is an autologous, self-blood product, an anticoagulated blood product generated by the centrifugation method of whole blood that primarily contains platelets at amounts up to 5 times those found in physiologic platelet concentrations. The use of PRP in pelvic floor reconstruction surgery is becoming much more common. To determine the efficacy of PRP on pelvic floor reconstruction surgery, we will synthesize the available research on the use of PRP for pelvic floor disorders.

Methods: This review was conducted on research articles in PubMed, Proquest, EBSCO, and ScienceDirect databases published between January 2010 – December 2023 regarding the use of PRP for pelvic floor reconstruction surgery. All primary research in humans, case reports and case series will be included to evaluate the outcome of PRP as an adjunct to conventional surgery in treating pelvic floor disorders.

Results: A total of five articles were chosen for review. Every article makes use of PRP in pelvic floor reconstruction surgery. Conclusions: This review offers actual evidence of PRP’s efficacy in pelvic floor reconstruction surgery. This is a new approach, and the findings of this study are expected to inform clinical practice and ongoing research focused on improving the outcome of pelvic floor disorders treatment.

Trial registration number: osf.io/gyr72

Keywords: Pelvic floor reconstruction; Platelet-rich plasma; Scoping review
INTRODUCTION

Pelvic floor disorders (PFDs), such as urine incontinence and pelvic organ prolapse (POP), can affect women of all ages and have a significant impact on their self-esteem and quality of life. Women are predicted to have a 1 in 4 lifetime risk of developing a PFD. PFDs are caused by increasing age, weight, parity, and a history of hysterectomy, and roughly 17% of women will be impacted at a certain time in life. Damage to the pelvic floor can result in incontinence (urinary and anal) and pelvic organ prolapse (POP) due to multiple pathophysiological causes. Treatment for incontinence or prolapse in women has been demonstrated to improve their quality of life and sexual satisfaction in studies.

Pelvic organ prolapse (POP) is a serious health disease that affects many women and can have a significant physical and psychological impact on their daily activities and quality of life. Pelvic organ prolapse occurs when the genitalia organ, bladder, rectum, and intestine protrude into the vaginal canal or even out of it. Urinary and bowel impairment, incontinence, and sexual dysfunction are the symptoms commonly develop. Although pelvic organ prolapse cannot result in major death or disease severity, it can reduce a woman's quality of life. Pelvic organ prolapse is a prevalent gynecological problem, with roughly 37% of patients seeking treatment in a clinic and a lifetime risk of 11-19% in the population for surgical operations.

Prolapse is a frequent condition caused by the weakening of the uterus supporting structures. The uterosacral (USL) and cardinal ligaments (CL) support the uterus and pelvic organs, while the round ligaments (RL) keep the uterus and pelvic organs in place. The connective tissue, smooth muscle, vascular, and innervation of the pelvic support systems are changed in women with pelvic organ prolapse (POP). The ECM (extracellular matrix) in connective tissue is primarily responsible for the supporting role of structures. The majority of the ECM is composed of fibrillar components including collagen and elastin, as well as non-fibrillar components such proteoglycans, hyaluron, and glycoproteins. Within this matrix, fibrillar components predominate over non-fibrillar elements, and collagen plays a significant role in the supporting function. According to a recent study, patients with POP had an inherent deficiency of a gene involved in the development of the USL. Collagen III and matrix metalloproteinase 1 (MMP-1) are overexpressed in the USL of women with POP, meanwhile there were decreased expression of collagen type 1 in uterosacral ligaments of women with POP.

There are various surgical management options are available to assist surgeons in pelvic floor reconstructions surgery. The surgery options include native tissue repair, mesh augmentation, and minimally invasive procedures. The type of surgical intervention performed is determined by the type of disorders identified during the evaluation and the related symptoms. Surgery for pelvic organ prolapse is usually successful in managing the
main symptoms of prolapse (vaginal bulge). Although the impact of pelvic organ prolapse surgery on certain bowel, bladder, and sexual functions can be predicted, individual women should be aware that the procedure can sometimes exacerbate existing symptoms or cause new ones, such as urine leakage or issues with sexual intercourse. Surgery techniques also have high frequency of postoperative complications and high recurrence rates, about 30% of patients require further surgery. Furthermore, when POP is treated without grafting, recurrence is common. Although the use of synthetic mesh or biological grafts provides structural reinforcement to POP weakened tissue, complications such as foreign body reaction, excessive fibrotic response, wound infections, and vaginal erosion are too common, necessitating surgical revision and, in some cases, mesh removal. These issues occur more frequently with vaginal mesh than with abdominal mesh, prompting two FDA warnings about the use of vaginal mesh in 2008 and 2011. As a result, new therapy strategies must be investigated as soon as possible. Implementation of cellular therapy with platelet-rich plasma (PRP), which would primarily strengthen the ligaments and speed up the healing process, could be an alternate technique for the therapy of pelvic floor disorders.

Platelet-rich plasma (PRP) is currently commonly used as a growth factor pool for promoting tissue regeneration in a variety of clinical settings, including orthopedics, ophthalmology, and healing therapies. Platelet-rich plasma is defined as plasma with a platelet count of more than 1,000,000/l in every 5 mL of plasma, as well as a variety of cytokines and growth factors. Platelet-rich plasma can be created using recently developed techniques. PRP is extracted from the blood of patients prior centrifugation. The separation of blood components (red blood cells, PRP, and platelet-poor plasma [PPP]) occurs after centrifugation and according to their distinct density gradients. There are a variety of procedures for collecting platelet concentrates, each of which might result in a different product with varied biology and applications.

PRP is a natural source of signaling molecules, and when platelets in PRP are activated, the P-granules degranulate and release growth factors and cytokines, which alter the pericellular milieu. Through growth factors and chemical mediators generated by platelets, platelet-rich plasma (PRP) can stimulate cell migration, proliferation, differentiation, angiogenesis, and tissue debris elimination. As a consequence, PRP may help improve tissue healing, regeneration, and repair. VEGF, IGF-I, PDGF, HGF, TGF-β, and FGF are some of the growth factors (GFs) found in PRP, and they all have a role in the pathophysiology of ligament restoration and that have been associated to the regeneration of collagenous tissue. During the early stages of tissue repair, these substances primarily stabilize the damaged tissue and direct local mesenchymal and epithelial cells to migrate, divide, and increase collagen and matrix synthesis, ultimately leading to fibrous connective tissue and scar formation. VEGF and FGF-2 are necessary for encouraging the development of new blood vessels to transport nutrients and progenitor cells to the damage site; although, neo-vascularization needs other substances.
IGF-1 in PRP is thought to improve early healing of ligament damage\textsuperscript{23}.

PRP is a viable therapeutic method for future regeneration treatments due to its relative ease of preparation, clinical application, favorable safety profile, and potential beneficial effect \textsuperscript{23}. PRP warrants proper consideration as an additional therapy for particular purposes due to its function in multiple healing pathways. A previous studies suggested that platelet-rich plasma is a promising technique for tissue repair and regeneration but studies into its clinical efficacy are not conclusive especially in pelvic floor disorders field. Looking at the bioactivity properties of PRP, we believe that PRP could provide a minimally invasive, low-risk, and effective treatment for pelvic floor disorders. To find primary studies on the use of PRP related to pelvic floor reconstruction surgery, a search will be conducted in the PubMed, Proquest, EBSCO and ScienceDirect databases. The findings of this study are expected to inform clinical practice and continuing research focused on improving pelvic floor disorders treatment.

METHODS

Study design

This scoping review will be carried out according to the Joanna Briggs Institute scoping review methodology and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) standards\textsuperscript{2526}. Scoping review is a method that addresses the underlying concepts surrounding the phenomenon of interest, offering a comprehensive overview that can be used as a foundation for systematic studies. Scoping reviews also show the depth and breadth of research on a topic, allowing for a better understanding of the phenomenon under study \textsuperscript{2728}. A scoping review, aims to map "important concepts, forms of evidence, and gaps in the research relevant to a given topic or field by systematically finding, identifying, and summarizing existing knowledge," as precursor to a systematic review\textsuperscript{2729}. This scoping review will be conducted using the Arksey and O'Malley methodology\textsuperscript{28}, with the optional sixth step omitted. The six processes are: 1. defining a research topic; 2. Locating relevant studies; 3. study selection; 4. data charting; 5. data collection, summarization, and reporting; and 6. Consultation exercise (ommitted).

Stage 1: identifying a research question

The Scoping review will systematically search the extensive literature regarding the use of PRP as an adjunct to reconstructive surgery (native tissue repair, minimally invasive surgery, mesh augmented etc) for pelvic floor disorders, as well as the factors associated with this intervention. The proposed scoping review questions are as follows:
1. What is known about the use of platelet-rich plasma in pelvic floor reconstruction surgery based on existing literature?
2. How the efficacy have been linked to using these interventions for pelvic floor disorders related to surgery treatment in the literature?

Stage 2: identifying relevant studies

Four databases will be used to find studies that are eligible: PubMed, Proquest, Ebsco, ScienceDirect databases. From January 2010 through December 2023, the search will be limited. A combination of medical search headings and free text words will be used to develop the literature search. Keywords will be selected and extracted from similar publications that are relevant to the study's population, topic, and setting. According to the database, the whole search will be performed using Boolean operators and proximity operators, including Medical Subject Headings (MeSH) terms, wildcards, AND, OR, parentheses, quotes, and more. The proposed search method for searching PubMed is shown in Table 1. This technique will be modified to fit the criteria of the other databases.

Table 1. Proposed search strategy to search PubMed

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<td>&quot;Pelvic Organ Prolapse&quot;[MeSH] OR pelvic-organ-prolapse*[tiab] OR urogenital-prolapse*[tiab] OR</td>
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<td>&quot;vesicovaginal fistula &quot;[tiab] OR rectovaginal fistula &quot;[tiab]</td>
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<tr>
<td>&quot;Hysterectomy, Vaginal&quot;[Mesh] OR &quot;Hysterectomy, Vaginal&quot;[tiab]</td>
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Stage 3: study selection

A two-stage procedure will be used to identify studies. After eliminating duplicate records, the titles and abstracts will be reviewed for potential eligibility by two reviewers using pre-specified screening criteria. Following that, papers that have been selected as relevant will be subjected to full-text review by both reviewers. Disagreements among the reviewers will be addressed through discussion or referral to a third reviewer. As recommended in the PRISMA extension for Scoping Reviews extension checklist, this information will be presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram, a schematic draft of which is presented as figure 1.

Inclusion criteria

All primary studies (including case reports, case series, randomised controlled trials, cohort, case–control, quasi-experimental, cross-sectional), all human and laboratory studies evaluating the outcome of PRP for pelvic floor reconstruction surgery will be included. Only article published in English language will be included.

Exclusion criteria

Studies that are irrelevant (including systematic, narrative and other review as well as conference abstracts, textbooks, posters and editorials) and not available in English language, it will be eliminated from selection.
Figure 1. Flow diagram research procedure

Stage 4: charting the data

Using a data extraction tool built by the reviewers based on scoping review instructions, data will be extracted from publications included in the scoping review. The extracted data will be electronically entered into the program using Microsoft Excel. The author(s), year of publication, country, subject investigated, design, interventions, and important findings pertinent to the study will all be included in the data extraction form. Two authors will independently extract information from all full-text papers selected for the final analysis. Discussion or referral to a third reviewer will be used to settle any disagreements or inconsistencies.

Stage 5: collating, summarising and reporting the results

Because this study is likely to produce both qualitative and quantitative data, data synthesis and analysis will be done using both a descriptive numerical summary and a theme analysis to characterize the current evidence base, including the scope of identified literature and the context of included research. The review will not comprise a meta-analysis, nor will the quality of evidence from included research be appraised. As a main
RESULT AND DISCUSSION

There was a total of 69 articles found. Mendeley software was used to find 13 articles that were identical, leaving 56 articles for title and abstract screening to find articles that matched the inclusion criteria. Because its topics did not focus on the use PRP for pelvic floor disorders, 45 articles were ruled out based on title and abstract screening, leaving 11 articles for full-text review. Only five articles were eventually included in the study based on the inclusion criteria.

The articles that were examined from Europe and America continent. Between 2012 until 2020, all of the investigations were published in journals. Two of the studies were in Italy, while the other were from Canada, Poland and Turkey. There were 3 cases of POP, 1 case of vesicovaginal fistula and 1 case of vaginal mesh exposure which underwent reconstructive surgery using PRP as an adjunct therapy with an observational study, in vitro study, case series and quasi experiment designs. Further details of each variable are given in Table 2. Table 3 summarizes the findings from articles regarding the objective of each studies, the population samples, the techniques procedure, the preparations and doses of PRP, as well as the results of procedures.

Table 2. Summary of the key characteristics of all included studies

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<tr>
<td>1</td>
<td>New approach in vaginal prolapse repair: minimally invasive surgery associated with application of platelet-rich fibrin</td>
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<tr>
<td>2</td>
<td>Attachment of Primary Vaginal Fibroblasts to Absorbable and Nonabsorbable Implant Materials Coated With Platelet-Rich Plasma: Potential Application in Pelvic Organ Prolapse Surgery</td>
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weeks following surgery in order to get autologous PRP. PRP or control media were coated on two meshes, absorbable (Vicryl) and nonabsorbable (Restorelle), and autologous PDP HVFs (n = 6) were seeded on meshes for 2 hours. The cells adhered to the meshes were fixed and counted after being stained with DAPI (4,6-diamidino-2-phenylindole dihydrochloride).


To see if autologous platelet-rich plasma (PRP) technology and a minimally invasive approach can be used to treat Exposure mesh following an ASC.

Three women with vaginal vault mesh exposure after laparoscopic ASC with concomitant hysterectomy

All of the women had endoscopic bipolar PlasmaKinetic resection (BPR) of the EM, and PRP gel was injected into the surgical site to fill in the gap created by the resection.

Using a 25-gauge spinal needle, the margins of the resected bed were infiltrated all around with PRP. PRP-G was injected into the surgical wound to fill the gap created by the resection.

RegenKit® technology (RegenLab SA, Le Mont-sur- Leman, Switzerland)

RegenKit-BCT tubes were centrifuged at 3250 rpm for 5 min and RegenKit-ATS for 10 min; 5 ml PRP

The average operating time was 39.6 minutes. In every case, surgery went perfectly. At the one-year follow-up, all of the women had regained sexual function, and no one had relapsed pelvic organ prolapse.

4 Cystocele Repair with Platelet-Rich Plasma to show the effectiveness of using Fifty six patients with cystocele

28 patients were operated with colporrhaphy anterior technique in a vacuum collection

A volume of 8 cc peripheral vein in a vacuum collection

The Pelvic Floor Distress Inventory scale showed a greater reduction in prolapse symptoms in group 2 (6 vs. 2, p = 0.002), the reoperation rate for symptomatic cystocele recurrence was significantly lower in group 2 (5 [17.8%] vs. 1 [3.5%], p = 0.001, and subjective success was significantly higher in group 2 (21 vs. 25, p = 0.012).


To see if a platelet-rich plasma (PRP) injection as a supportive treatment for recurrent VVF surgery is effective.

16 patients with recurrent VVF

The PRP was injected transvaginally and via cystoscopy. PRP was injected at 4 to 5 points around the edges of the fistula. 6–8 weeks after the PRP injection, a surgical Latzko operation for VVF closure was scheduled.

The patients’ whole blood (150–180 mL) was collected into sodium citrate tubes (ratio 9:1). An Artrexs Angel System® kit (Artrexs Inc., Naples, USA) was used to centrifuge the tubes, yielding PRP quantities of 4–6 mL

1 patient had the fistula self-healed after 2 weeks of PRP injection. All other patients were checked 4 to 6 weeks following the Latzko surgery and remained dry during that time. The vaginal wall at the operation site healed without any scarring, redness, or granulosa tissue in all cases. Furthermore, no urological problems or urinary tract diseases were reported by the patients. Furthermore, all patients’ postvoid residuals were less than 50 mL.
The majority of women who have POP surgery will have reconstructive surgery to address problems in the anterior compartment (bladder and urethra), apex (uterine or post hysterectomy vault prolapse), and/or posterior compartment (perineum rectocele or enterocele) 35. Autologous tissue repair surgery and scaffold implantation surgery are currently the most regularly used surgical procedures in clinical practice. Because autologous tissue repair has a high recurrence rate, pelvic floor reconstruction focuses on mesh insertion. Unfortunately, polypropylene mesh was banned in 2019 after the FDA warned of problems like erosion and exposure, 36. Finding therapy options that will assist patients in improving pelvic support is critical. The use of cellular component technology for female pelvic floor repair was born as a result. The use of PRP in the field of female pelvic floor surgery is, however, rarely examined. We discuss the application of PRP in the field of female pelvic floor dysfunction surgery in the hopes of providing theory to guide the treatment of pelvic floor dysfunction.

We have identified 5 articles discussed the use of PRP in pelvic floor reconstruction surgery procedure. PRP preparations and various protocols have been used as complementary modalities to surgery in the treatment of pelvic floor disorders. There were three studies that discuss the use of PRP in pelvic organ prolapse surgical procedures. The idea of administering PRP to treat POP originated from PRP’s ability to increase collagen concentration in fibrous connective tissue since pelvic organ prolapse has been linked to a lower collagen concentration in the pelvic floor muscles, ligaments and other supporting tissues when compared to healthy individuals and PRP also improving wound healing 37. More notably, Gorlero et al examined the efficacy of platelet-rich fibrin (PRF) in 10 patients who had vaginal surgical operations due to prolapse recurrence using the Vivostat system. The authors found an anatomical success rate of 80%, with patients reporting a 100% improvement in symptoms and a 20% increase in sexual activity 30. Based on the findings, the authors recommend using the PRF system as the best treatment for patients who are at risk of recurrence or erosion. Similarly, Atilgan et al investigate the efficacy of platelet-rich plasma in cystocele correction. They performed 4 ml PRP injection into the pubocervical fascia concurrently with colporrhaphy anterior procedure. They found that Platelet-rich plasma injection during cystocele repair group were more significant for the reduction in prolapse symptoms as measured by the Pelvic Floor Distress Inventory scale (6 vs. 2, p = 0.002), the lower reoperation rate for symptomatic cystocele recurrence (5 (17.8%) vs. 1 (3.5%), and increase subjective success evaluated with Patient Impression of Global Improvement Scale (21 vs 25, p=0.012). During the 48-month follow-up period, they didn't notice any side effects from PRP therapy 33. They conclude that platelet-rich plasma treatment may be a feasible alternative for preventing cystocele recurrence.

Recurrent prolapse is prevalent, with 29% of women having to have at least one reoperation 38. Due to the poor results, the repair has been supplemented with a variety of
materials, including synthetic and biologic grafts. Various transvaginal mesh implants have been introduced in pelvic floor reconstructive procedures to lower the recurrence risk. Different types of vaginal implants, both absorbable and nonabsorbable, used in pelvic floor reconstruction surgeries have to many major side effects. Pain, mesh erosion and infection, vaginal bleeding and discharge, and fistulas are only just few symptoms. Platelet-rich plasma is known contain many growth factors that increase cell proliferation and attachment in vitro. Medel performed invitro study to investigate the attachment of primary HVFs on vaginal meshes precoated with autologous PRP in vitro. The authors found that after coating PRP compared with Dulbecco modified Eagle medium, POP Human vaginal fibroblast (HVF) attachment to both meshes was significantly increased (Vicryl: 9875 vs 1006 cells/cm2, Restorelle: 3724 vs 649 cells/cm2; P 0.001 for both). They conclude that when primary POP HVFs are treated with PRP, cells have a better attachment to implant materials, which could lead to less mesh-related problems in vivo, indicating that it has a lot of potential for urogynecologic procedures.

The results of study conducted by Medel et al provide a choice of therapeutic strategies for complications that may arise in the use of implant materials in pelvic floor reconstruction surgery. For example in procedure sacrocolpopexy for apical prolapse treatment, the prevalence of vaginal mesh exposure after this procedure ranges from 2% to 8%, prompting surgery in many cases, particularly in symptomatic patients. When treating it, it's important to remove the exposed mesh (EM) completely to accomplish vaginal closure while preserving as much vaginal tissue as possible to avoid a shorter and narrower vagina. Castellani et al. presented their preliminary findings in three symptomatic women who had vaginal mesh exposure after abdominal sacrocolpopexy and were treated with endoscopic mesh excision with a resectoscope, followed by PRP application on the resected surface and PRP-gel injection around it during the same procedure. Six months after surgery, there was complete re-epithelization, and one year later, there was remission of preoperative symptoms and no prolapse. Based on the results, they argue that combining bipolar PlasmaKinetic resection (BPR) and PRP for treating vaginal mesh exposure while preserving anatomical results and sexual function is a safe, effective, simple, and feasible technique.

The use of PRP in the repair of vesicovaginal fistulas (VVF) has also been studied. The use of PRP comes from its well-known wound-healing potential. The bioactive factors in platelets are found in the alpha-granules and dense granules. Growth factors and cytokines are found in the alpha granules. Serotonin, histamine, dopamine, calcium, and adenosine are all found in the dense granules. Cell proliferation, chemotaxis, cell differentiation, and angiogenesis are all facilitated by these growth factors and cytokines. The biological aspects of tissue repair are fundamentally affected by these nongrowth factors. Streit-Cleckliewicz et al. administered PRP to 16 patients' fistulas at a 6–8 week interval before performing the Latzko surgery for VVF repair. After PRP injection, one patient (1/16) was cured and did not
require surgery. There were no adverse events reported, and the remaining patients reported complete dryness and no urinary problems during the follow-up period, demonstrating the safety and efficacy of the combined PRP and surgical therapy.
CONCLUSION

Based on scoping review of the articles, we conclude that the use of Platelet-rich plasma (PRP) in Pelvic floor reconstruction surgery has three primary roles:

1. Platelet-rich plasma (PRP) is a type of plasma that improves in wound healing. This phenomenon is related to the fact that it increases the mitogenesis of healing-capable cells as well as tissue angiogenesis by growth factors. This PRP effect can be used to promote the healing process such as in fistula repair procedures.

2. Many growth factors, chemokines, and cytokines are known to be present in PRP, which activate downstream signaling pathways that contribute to the formation of proteins required for collagen and extracellular matrix synthesis. PRP helps to repair broken connective tissue by increasing fibroblast migration, proliferation, and activation. PRP preparations also help to revascularize injured tissue by encouraging endothelial cell migration, proliferation, differentiation, and stability in new blood vessels. These PRP functions may use to prevent recurrence prolapse in native tissue repair for POP surgery.

3. PRP contains several cell adhesion molecules, such as fibrin, fibronectin, vitronectin, and thrombospondin, which cause vaginal fibroblasts and epithelial cells to integrate. This profile allows the use of PRP in pelvic floor reconstructive procedures that using implant material to increase the outcomes and reduce the adverse effect.

Demerit of the use of PRP products in pelvic reconstruction surgery is there were large diversity of PRP preparations and application methods. The preparation kits and equipment used, the amount of harvested blood sample, the technical details of preparation (centrifugation components), type of application, activation method, all differ significantly among the included studies. We propose characterizing the type of PRP utilized in each of the ongoing research, with the goal of standardizing PRP so making it easier to sort and interpret the data.
REFERENCES


