

## Pentosan polysulfate maculopathy versus age-related macular degeneration



Interstitial cystitis is an incompletely understood syndrome of chronic suprapubic pain and irritative voiding symptoms (dysuria, urgency, frequency and nocturia). The population prevalence is estimated to be around 11 per 100,000 and it is 6 times higher in women than men.<sup>1</sup> Pentosan polysulfate sodium (PPS), a semi-synthetic carbohydrate derivative, was approved in 1993 by Health Canada for the treatment of interstitial cystitis, and is the only oral medication approved for this indication.

In 2018, Pearce and colleagues published their landmark description of a novel pigmentary maculopathy in patients taking PPS.<sup>2</sup> The condition presents most commonly with reading difficulty and nyctalopia and manifests clinically with parafoveal hyperpigmented RPE changes surrounded by subtle yellow-orange subretinal deposits. Fundus autofluorescence is distinctive, showing a circumscribed area of irregular hyper- and hypo-autofluorescence located in the posterior pole. The association was corroborated by other investigators. Consequently, in 2020, Health Canada released a safety alert for PPS recommending that prescribers warn patients about the risk of maculopathy, arrange baseline and regular follow-up ophthalmic examination for those taking it, and avoid prescribing to patients with pre-existing macular disease.<sup>3</sup>

Ophthalmologists have a crucial role in defining evidence-based screening strategies for patients at risk of PPS maculopathy. Areas of uncertainty include detectability of pre-symptomatic disease, natural history of the condition

and how this is affected by drug discontinuation, safe dosing limits and whether other factors modify the risk of developing maculopathy.<sup>4</sup> Until these questions are definitively answered, ophthalmologists might consider liaising with colleagues in urology and gynaecology to ensure there is a robust referral process for patients about to start the medication and for those who develop visual symptoms while taking it. It would also seem sensible, where possible, to assess for a history of PPS use in patients currently being followed for macular disorders, as some of these patients may have been misdiagnosed.

In this issue of CJO, Christiansen and colleagues addressed the latter subject by exploring multimodal imaging features helpful in distinguishing PPS maculopathy from age-related macular degeneration.<sup>5</sup> Their criteria for categorizing patients as having PPS maculopathy showed high inter-rater agreement. Interestingly, none of the patients classified as having PPS maculopathy had typical drusen, making the latter much more suggestive of AMD. Furthermore, in patients classified as having AMD or drusen, exposure to PPS was associated with more hyperpigmentary changes. It should be noted that, while case reports exist of macular neovascularization in patients with PPS maculopathy, RPE atrophy appears to be the predominant cause of vision loss in this condition.<sup>6</sup> Cessation of therapy is currently the best management strategy for these patients, although vision loss and RPE atrophy may progress after cessation. If neovascularization develops, it has been found to be treatable with anti-VEGF agents.

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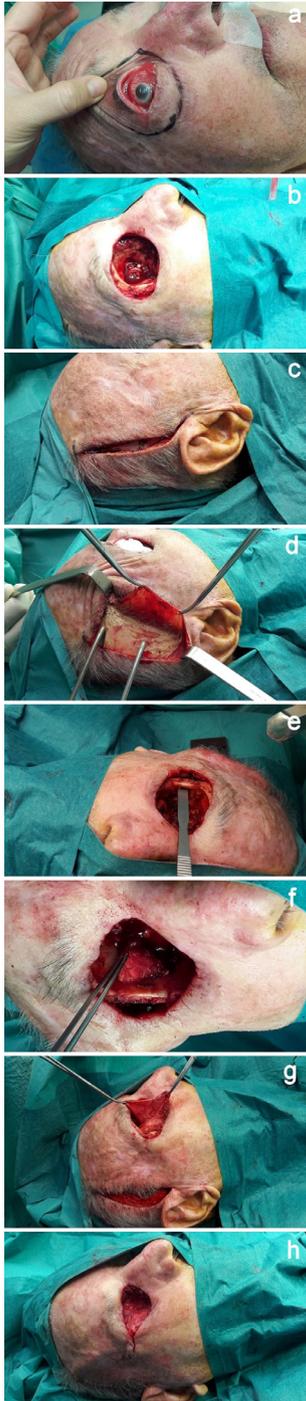
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## Total orbital exenteration with temporalis muscle transfer and secondary healing



Healing of the orbital socket after total exenteration can be achieved either by 1) spontaneous granulation, associated with healing by secondary intention, or 2) the use of a flap or a graft. Spontaneous granulation results in a prolonged healing process so it should be avoided, especially in patients with 1) a history of neoadjuvant radiotherapy that can delay the recovery process further, and 2) anticipated adjuvant radiotherapy after surgery. Given that a significant portion of exenteration patients receive neoadjuvant or adjuvant radiotherapy, there has been much research interest in the utility of a flap or graft in facilitating the healing process. In this issue of CJO, Lemaître and colleagues explore the utility of an ipsilateral temporalis muscle flap after total exenteration for ophthalmic tumours.<sup>1</sup>

This was a single centre retrospective study that included all patients who underwent total exenteration for an ophthalmic malignancy with a single stage repair using a temporalis flap between 2009 and 2016. For all patients, after transferring ipsilateral temporalis over to the site of exenteration, the anterior surface of the muscle flap was left to heal by secondary intention. The following data were collected: sex; age; histologic tumor diagnosis; complete or incomplete excision on histology; time to complete epithelialization; data regarding the neoadjuvant and adjuvant orbital external beam radiotherapy; orbital tumor recurrence after exenteration; occurrence of metastases; patient survival; and postoperative complications.

The 29 patients enrolled in the study included: 18 conjunctival melanomas, 2 choroidal melanomas, 6 squamous cell carcinomas, 2 sebaceous cell carcinomas, and 1 basal cell carcinoma. Mean age at surgery was 70.7 years. On histological exam, tumour excision was complete in 25 patients. Of these, 3 had insufficient negative margin and required adjuvant orbital radiotherapy; none had recurrence post radiotherapy. Another 3 patients who had conjunctival melanomas developed local recurrence despite sufficient negative margins. Meanwhile, 4 of the 29 patients had incomplete tumour excision (positive margin). While 3 underwent adjuvant radiotherapy with no subsequent orbital recurrences, radiotherapy was unable to be performed in the fourth patient given his poor general health. Twelve patients had history of neoadjuvant radiotherapy. The mean time to epithelialization was not significantly different ( $p = 0.25$ ) between the patients who received neoadjuvant radiotherapy (6.2 weeks) versus those who did not (9.2 weeks).

Four patients developed post-operative complications: 2 sino-orbital fistulas, 1 flap necrosis with subsequent sino-orbital fistula, and 1 orbital cyst. All patients were fitted with prostheses and were satisfied with aesthetic outcomes.

Previous studies have reported the healing time in exenteration to be between 5 to 11 months with spontaneous granulation, 10 months with a split skin graft, and 6 weeks with dermis fat graft. Lemaitre and colleagues demonstrated that the time to epithelialization is as short as 7.9 weeks with a temporalis flap, markedly shorter than spontaneous granulation and split skin graft. This reduced healing time allows for early postoperative radiotherapy. Given that the adjuvant radiotherapy was indicated in as many as 7 of the 29 (24%) exenteration patients, either due to insufficient or lack of negative margin, the ability to start postoperative radiotherapy as early as possible can reduce the risk for interval growth, local spread, and metastasis of the residual tumor. Another advantage of temporalis muscle flap is reduction in hyperostosis of the socket, which can be misdiagnosed as tumor recurrence or infection. Lastly, temporalis flap reduces the risk for osteoradionecrosis in the patients with history of neoadjuvant radiotherapy, which was given to a significant portion (12/29; 41%) of exenteration patients.

The surgical technique for the temporalis flap used by Lemaitre and colleagues is unique compared to the temporalis flaps documented in previous reports. Their technique involves allowing the anterior surface of the muscle flap to heal by secondary intention, as opposed to covering the

muscle flap with a cutaneous advancement flap or a skin graft. This novel approach allows for a shorter procedure time and early detection of local tumor recurrence on clinical exam in comparison to the previous temporalis flap techniques; good cosmesis; low rate of complications (only 1/29 with flap necrosis); and all the aforementioned benefits of temporalis flap over spontaneous granulation.

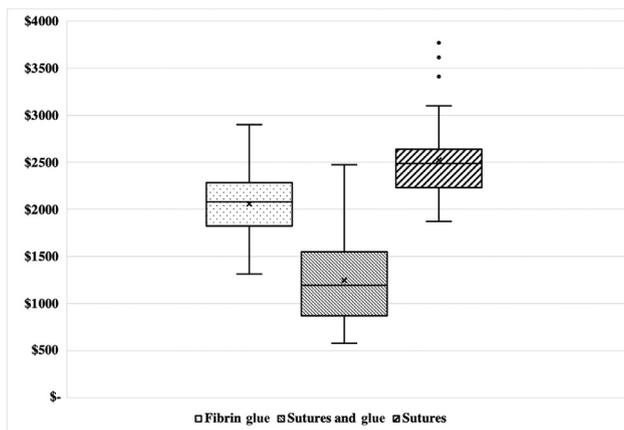
To conclude, this study presents a novel approach to total orbital exenteration with temporalis muscle transfer and secondary healing of the anterior surface of the flap. The surgical technique outlined in this study provides significant benefits and minimal risks when compared to the exenteration techniques utilizing spontaneous granulation, skin graft, and also the temporalis flap from previous reports. Therefore, this paper makes significant contribution to the growing body of literature and the care of patients with aggressive ophthalmic malignancies.

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## Fibrin glue in pterygium removal surgery



Pterygium is the fibrovascular conjunctival growth extending over the cornea. Surgical removal is the mainstay for treatment when they cause visual disturbance including astigmatism, chronic foreign body sensation, redness, or cosmetic concerns.<sup>1</sup> One method for preventing recurrence is to fix a conjunctival autograft to the wound bed either using sutures or fibrin glue, which have their respective pros and cons. Studies have found

fibrin glue to be as effective as sutures and may have less recurrence, shorter healing time, and a shorter procedural time.<sup>2,3</sup>

This is particularly relevant in the current era of “Choosing Wisely” and the Iron Triangle. Great emphasis is being placed on maximizing resource utility and stretching the healthcare dollar, while maintaining patient-centered quality of care.<sup>4,5</sup>

In this issue, Soumaya and colleagues conducted a timely cost-effectiveness analysis through a retrospective chart review comparing fibrin glue and sutures in pterygium conjunctival graft fixation at a Canadian tertiary care center.<sup>6</sup> The total cost of equipment, surgeon remuneration and cost of operating room utility were calculated in Canadian dollars (CAD). Data was collected from patients who underwent suture-only (10-0 Nylon) fixation between January 2008 to January 2010 and from patients who underwent fibrin glue with or without sutures from April 2017 to 2018. The calculated operating cost was \$51.20 per minute, which included remuneration for OR staff.

A total of 164 eyes from 153 patients were included. Of these, 55 used fibrin glue, 50 used both glue and sutures for a dual technique, and 59 used sutures alone for autograft fixation. The demographics of patients' age and sex were similar across these groups. Interestingly 94% of fibrin glue cases had a surgical assistant (resident or fellow) present, compared to 76% and 49% in the dual technique and suture-only cases, respectively. There was also a difference in the average years of surgeon's experience

between the groups, with the dual technique group having more years of experience.

The results show that average total cost of the fibrin glue method was \$2063 +/- 660.60 CAD and the suture-only method was \$2528.90 +/- 385.60 CAD. This indicates a total cost savings of around \$600 to \$750 per procedure. Furthermore, the fibrin glue method allowed for 18 cases per average OR day compared to 13 cases with sutures alone. In calculating the relative cost proportions of pterygium surgery, in all 3 groups, the most costly component was the cost of the operating room, followed by surgeon's remuneration and cost of equipment. Cases that were completed with sutures alone showed 72% of total expenses were associated with OR maintenance.

Interestingly, the dual technique method was both more time-efficient, allowing for 22 cases per OR day and more cost-efficient, costing a total of \$1846.80 +/- 402.30 CAD per case. This could be an interesting area to investigate further.

There are a few limitations to this study. Firstly, there are limitations inherent to a retrospective review as well as a limited sample size. Furthermore, there is imbalance in the surgeons' experience and presence of a surgical assistant between the groups that could confound results. A difference of almost 10 years in between the data collected from the suture-only and fibrin glue groups may be another confounding variable. Future directions could include patient satisfaction surveys and accounting for transportation costs for follow up appointments for suture removal, for instance.

In summary, this study is among the first to complete a cost-effectiveness analysis comparing these two approaches. Bouhout and colleagues suggest that conjunctival autograft fixation in pterygium surgery using fibrin glue only could be a more cost-effective approach compared to sutures alone, as overall surgery costs

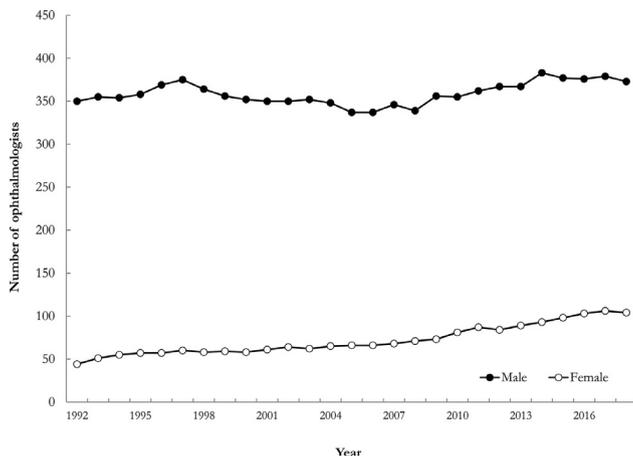
are reduced through decreased procedure time. Additional studies are required to address the limitations of this study with respect to confounding variables and prospective long-term follow up.

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## Trends in payments among male and female ophthalmologists in Ontario



In recent years, there has been much focus on and discourse surrounding the issue of the gender wage gap. This gender wage

gap persists in Canada for all occupations, including for physicians, despite a healthcare system based on, for the most part, a fee-for-service model.<sup>1,2</sup> The gender pay gap is a result of a variety of factors. For example, differences in productivity is one such contributing factor. However, a publication by Buys et al. in 2019 showed that after adjusting for volume of patient visits and number of distinct patients, the pay gap by sex still remained significant for all physicians except family physicians. In particular, the female-to-male pay gap increased in more recent cohorts for ophthalmologists.<sup>2</sup>

In this issue, Buys and colleagues explore this unexplained sex billing gap among Ontario ophthalmologists.<sup>3</sup> Using ICES databases, a retrospective review of ophthalmology patient visits in Ontario from 1992 to 2018 was conducted. Data was also analyzed by full-time equivalent (FTE) as a measure of workload, where they defined 1.00 FTE as yearly payments between the 40th to 60th percentiles, <1 FTE as below the 40th percentile, and >1 FTE as above the 60th percentile.

From 1992 to 2018, while overall median yearly payments increased, median payments for male ophthalmologists were

greater than for females during this period ( $p < 0.0001$ ). There was an unadjusted billing gap of 25.7% in 2017 (45.3% in 1992 and 26.9% in 2018). However, the female-to-male payments ratio increased from 55% to 73% in that same time. Furthermore, when examining by FTE, the pay gap was not significant in the 1 FTE group. In the  $<1$  FTE group, females billed less than males in 1992 but more in 2018. These billing patterns were reversed for the  $>1$  FTE group.

Proportionally more female ophthalmologists fell into the  $<1$  FTE group, which accounted for part of the wage gap. But why are there more females within the  $<1$  FTE group? A survey by McAlister et al.<sup>1</sup> reported that female ophthalmologists may more frequently take up family/childcare and household responsibilities; though, these responsibilities are unlikely to be the reason in the current review, as the average age of ophthalmologists (of both genders) was highest in the  $<1$  FTE group. There has been the suggestion that a so-called “confidence gap” predicts gender pay gaps among graduates in the science, technology, engineering, and math (STEM) fields.<sup>4</sup> Self-beliefs about one’s abilities can potentially affect clinical opportunities and workload. Buys et al. suggest that differences in workload/productivity by gender may be secondary to referral complexity, nature of the referral (surgical need) and opportunities to operate, and billing practices. Female physicians may receive more complex referrals that require more time per patient.<sup>5</sup> Male ophthalmologists have been reported to have more operating time than female ophthalmologists<sup>6</sup> and a higher proportion of male ophthalmologists perform surgery than females (68.6% vs. 57.9%).<sup>7</sup> Female surgeons have also been reported to bill less aggressively compared to their male counterparts.<sup>8</sup> Reasons for these differences are not entirely known.

Buys and colleagues acknowledge that the current review did not consider physician factors such as socioeconomic status, race, and practice patterns, among other things. Social constructs and unconscious biases may also play a role. It is clear that the gender pay gap, both as a whole and within ophthalmology, is complex. Identifying barriers and

obtaining a greater understanding of the variables contributing to this disparity are needed in order to eliminate the gender pay gap.

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