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Hyperbaric oxygen for radiation cystitis

Delayed cystitis secondary to therapeutic radiation is an uncommon but serious complication that, in its most serious expression, is likely to require multiple serial blood transfusions and can even be lethal. Treatment with chemical and electrocautery is frequently employed but the cystitis is subject to frequent recurrence. In *The Lancet Oncology*, Nicklas Oscarsson and colleagues[1] present the results of a randomised, controlled trial reporting the effects of hyperbaric oxygen therapy in the treatment of moderately severe radiation-induced cystitis. This work is the culmination of years of effort in recruiting patients by five Nordic university medical centres to this well-designed and very important trial. Eventually, and not including patients who withdrew immediately after randomisation, 41 patients assigned to hyperbaric oxygen therapy and 38 controls were available for intention-to-treat analysis. All but one patient in the intervention group completed their course of hyperbaric oxygen, consisting of 30–40 daily treatments at 240–250 kPa for 80–90 min of 100% oxygen at pressure. Patients in the control group received standard care, the nature of which was not specified in the study report. Primary outcome measures consisted of self-assessed urinary symptoms before and 4–6 months after therapy assessed with the Extended Prostate Index Composite (EPIC) score, and general health-related quality of life assessed with 36-item Short Form (SF-36) questionnaire. Additionally, cystoscopies were done before and after the intervention, with findings from the gross bladder mucosa assessed by urologists masked to treatment assignment and compared with the Radiation Therapy Oncology Group's Morbidity Grading System. Biopsies of the bladder mucosa were also taken to be analysed and reported later.

At follow-up, self-assessed urinary symptoms and health-related quality of life (general health on the SF-36) and the gross morphological grading of bladder mucosa, were significantly different in favour of the intervention group. The hyperbaric oxygen therapy group improved by a mean of 17·8 points on the 100-point EPIC urinary total scale compared with a mean improvement of only 7·7 points in the control group (difference between group means 10·1 points [95% CI 2·2–18·1], p=0·013). Although not a part of the original study design, patients in the intervention and control groups who were also affected by radiation proctitis had their EPIC bowel scores compared before and after treatment. This analysis also showed significantly improved results in the hyperbaric oxygen therapy group compared with the control group.

The investigators state that their study design was inclusive but also pragmatic. They discuss the potential criticism that their design was not masked except for the gross morphometric assessment of the bladder. They note that other hyperbaric oxygen therapy trials have been masked, but at least some have been affected by poor recruitment, and all have required extensive commitment of scarce resources. Certainly, the placebo effect is well known. However, in these patients who had been affected by radiation-induced cystitis for several years, in delaying the assessment of the primary outcome for 4–6 months after hyperbaric treatment, any placebo effect would likely have faded from the patient's mind. A Cochrane analysis[2] of placebo-controlled trials shows that perception—and not physiological improvement—is at the heart of the placebo effect.[2] Another potential criticism is that patients in the control group were allowed to cross over after the primary outcome assessment at 6–8 months after randomisation, and nearly all did so. Recall again that these patients had had symptoms for approximately 3 years on average and the natural history of this disorder had already been well established. Chong and colleagues[3] have

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reported improved success in treating patients with radiation-induced cystitis when the symptoms have been less than 6 months in duration, suggesting that results of this trial might have been even better if earlier intervention had been used.

Issues not answered by this trial are the optimal course of hyperbaric oxygen therapy, including the best treatment pressure, the optimal duration of 100% oxygen at pressure, and the appropriate number of treatments. Some patients in the study were treated with oxygen for only 80 min; meanwhile, some received only 30 treatments. The works of Marx, Hampson, and Feldmeier[4–6] suggest 90 min of 100% oxygen at 2·4 atmospheres absolute for a minimum of 40 treatments. On the basis the work by Oscarsson and colleagues and my many years of experience, I recommend these standards and advise against anything fewer than 40 treatments, pressures less than 2·4 atmospheres absolute (approximately 240 kPa), and time on 100% oxygen less than 90 min.

Finally, investigators, including myself, have observed that a sizeable proportion of patients treated with hyperbaric oxygen therapy for radiation cystitis will have symptom recurrence even after an apparently adequate course of therapy, but can often be salvaged with additional hyperbaric oxygen treatments.[6,7] Long-term follow-up in patients from this study will be essential to establish the durability of response to hyperbaric treatment and the need for additional treatments. It is important to remember that other so-called standard treatments are subject to disease recurrence and often need to be repeated.[8] Moreover, the only true definitive treatment for this group is cystectomy and urinary diversion, with this surgery resulting in a substantial deterioration in quality of life. Importantly, in its most serious presentations, radiation cystitis can be fatal.[9]

I applaud the investigators for their well-done study that establishes level 1 evidence in support of hyperbaric oxygen therapy for delayed radiation cystitis.

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I am Past President of the Undersea and Hyperbaric Medical Society. I declare no competing interests

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Moonshot or groundshot: addressing Europe's cancer challenge through a patient-focused, data-enabled lens

The latter half of 2019 has been a major inflection point for cancer control in Europe, with renewed focus and energy from myriad stakeholders. On Sept 12–14, the European CanCer Organisation (ECCO), representing 27 pan-European cancer organisations and with 17 patient organisations at its heart, held its annual Cancer Summit. A series of resolutions were passed, emphasising the need to boost cancer prevention and control in all European countries, based on principles first articulated in the European Cancer Patient's Bill of Rights (BoR).[1] The following week, the newly elected European Parliament held a lively debate on "The Fight Against Cancer". At the European Society for Medical Oncology Congress in Barcelona (the largest cancer congress in Europe with more than 30 000 attendees), the public policy track, in collaboration with WHO, emphasised the need for improved cancer care across all of Europe. September also saw the publication in