Treatment of Abdominal and Pelvic Radiation Injury

I read with interest the retrospective review by Feldmeier et al. (1) on the use of adjunctive hyperbaric oxygen (HBO₂) in delayed radiation injuries of the abdomen and pelvis. In our facility we see a number of similar injuries and we are encouraged by the findings of this review. Dr. Feldmeier and his colleagues are to commended; however, it may be useful to consider some aspects of the review which may modify the confidence with which we draw any conclusions.

The period of review is relatively long (17 yr) if the last patients were entered in 1996. The grouping of patients over time always runs the risk of obscuring the effect of changing treatment or disease, particularly if the study group is then used as comparison for a contemporary group. Patients enrolled and treated today may not have much in common with those patients treated in 1979. It is not clear in what way this will affect HBO₂, surgery, or any treatment.

The authors quote an overall success rate of 81% in those receiving at least 20 treatments. This figure is presumably derived from the numbers known to be healed (26) and those known to have failed to heal (6). Although this is accurate in an arithmetic sense, it runs the risk of being misinterpreted as a stronger association than may really exist. For the sake of clarity, it might have been advisable to quote an overall figure for healing rate as 59.4% of the whole group (26 healed out of 44 cases). Those lost to follow-up or having incomplete treatment will not be identifiable when considering HBO₂ for an individual patient, and so the demonstrable chance of healing with HBO₂ for them is 60% rather than the 80% it may be after successful completion of the treatment course. It is analogous to excluding from analysis patients in a drug trial who suffer side-effects and refuse to continue therapy. This is a violation of the epidemiologic principle of "analysis by intention to treat" and can produce misleading results (2).

The relative efficacy of HBO₂ in these cases is difficult to quantify without a measure for the rate of successful healing in a cohort of patients who were not offered HBO₂. The reviews of Mathes and Hurwitz, Fisher et al., Hamberger et al., or others quoted may contain such information but the figures are not directly offered in this paper. Do the authors have a feeling for the base rate of healing without HBO₂? It is possible the comparisons made on the rates of operative intervention are misleading, as the authors suggest. The indication for operation may be successful periwound revascularization.

I commend the authors for their work in producing this very encouraging review and we all look forward to prospective studies to confirm these findings.

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The Authors Respond:

We have read Dr. Bennett's letter and appreciate his kind words in regard to our report. Dr. Bennett raises several issues that we believe deserve our response.

1. Dr. Bennett suggests that we include all patients in the analysis, even those who had fewer than 20 treatments or were lost to follow-up. We restricted our analysis to patients who had what we considered to be an adequate course of therapy and in whom follow-up was available. All the raw data were included in the extensive tables so the readers could draw their own conclusions. If we evaluate those patients whose healing was not documented, we find the following: three were lost to follow-up; 10 patients were discontinued with as few as three treatments due to recurrent malignancy or other intercurrent disease. Only two patients refused to continue treatment. Three additional patients were failures; one died from radiation therapy and two improved but did not heal. For years the hyperbaric community has been striving to have oxygen considered as a drug. It is axiomatic that this drug as any other should be given in adequate doses for an appropriate period of time if we are to expect a favorable outcome. The vast majority of patients in our report who did not compete therapy did so for reasons unrelated to HBO₂ and not as a result of toxicity or intolerance to HBO₂.

2. Dr. Bennett also suggests the long period for patient inclusion might be misleading. The implication is that something has happened to alter the pathophysiology of delayed radiation injury. The pathophysiology of delayed radiation injury has not changed since the introduction of
cobalt therapy in the 1950s and linear accelerators in the
1960s. With more targeted confirmal therapy, the fre-
quency of radiation injury is expected to decrease, but for
any given injury the mechanism for that injury has not
changed.

3. Dr. Bennett also inquires as to what the outcome of
such patients would be without HBO₂. In this series of
patients, as in other series of late radiation injury, the
problems were chronic. Several patients had suffered with
their injuries for years or even decades before their referral
for HBO₂. No other effective therapies for radiation injury
are known except for resection or bypass of the affected
organ. Surgical intervention is also subject to poor outcome
with high incidence of anastomotic leaks, wound infections,
and dehiscence (1). There are no good numeric reports of
outcome other than small retrospective reviews. In the most
severe cases there is a significant incidence of lethality (as
high as 25%), and to quote Rubin and Casarett (2) in their
classic work on radiation pathology, "... the majority of
these cases do poorly."

It is our belief that it was reasonable to modify the
discussion of outcome to include only those patients who
had received an adequate oxygen dose and who were
available for follow-up. Ideally, this issue should be
subjected to a prospective clinical trial. Because delayed
injuries of the abdomen and pelvis are uncommon, it will
take the cooperation of many centers to accomplish such a
prospective trial. In the absence of large prospective
clinical trials, retrospective reviews and well-controlled
animal studies can offer some guidance (3).

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REFERENCES
1. Morgenstern L, Thompson R, Friedman NB. The modern enigma of
134:166–172.
3. Feldmeier JJ, Jelen I, Davolt DA, Valente PT, Meltz ML, Alecu R.
Hyperbaric oxygen as a prophylaxis for radiation-induced delayed