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LETTER TO THE EDITOR

Prophylactic octreotide in pancreatoduodenectomy: response to Yang *et al*.

We appreciate the comments of Yang and colleagues on our recent work entitled 'Prophylactic octreotide for pancreatoduodenectomy: more harm than good?'[1] We agree with several of their points, particularly that the current evidence in the translational literature directly linking octreotide to the formation of fistulas is far from definitive; however, defining the mechanism of fistula development in the setting of prophylactic octreotide was beyond the scope of our paper. Despite this, we cited over 15 studies that may explain our clinical findings.

Secondly, although our findings contrast with those of several randomized controlled trials (RCTs), each of those studies predated the advent of the International Study Group on Pancreatic Fistula,[2] which established definitions for clinically relevant postoperative pancreatic fistula (CR-POPF) through international consensus. In fact, although the differences were non-significant, the only RCTs to be conducted since those definitions were published have reported higher rates of fistula formation with octreotide.[3,4] The overall fistula rates in our study (octreotide group: 28.1%; control group: 21.5%) compare favourably with those in the most recent RCT (octreotide group: 25%; control group: 18%).[4] Contrasting findings were recently reported with the new somatostatin analogue, pasireotide, but the efficacy of this drug has not been tested in a multicentre fashion.[5]

Lastly, a forthcoming study by our group of outcomes in over 4300 pancreatoduodenectomies performed by 55 surgeons at 15 institutions found octreotide to be associated with a greater incidence of CR-POPF [odds ratio (OR) 3.3; $P < 0.0001$] similar to the figures reported in our recent paper (OR 2.6; $P < 0.001$).[1] The later study controlled for elements of endogenous and operative risk, as well as for mitigation strategies (octreotide, drains, stents, etc.), institutional volume and surgeon experience. An important takeaway from that analysis, and our paper on octreotide,[1] is that fistula risk is multifactorial; octreotide was associated with elevated CR-POPF rates, but other factors also rose to statistical significance. We believe it is imperative to control for all components of CR-POPF risk when evaluating the efficacy of fistula mitigation strategies.

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