Comment

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Laparoscopic cholecystectomy in England and Wales: results of an audit by The Royal College of Surgeons of England

We write to express concern at a current trend wherein the fundamental principles of scientific research and the values of clinical audit have become confused. This was highlighted in a recent audit of laparoscopic cholecystectomy published in this journal (*Annals*, July 1994, vol 76, p269). The authors have undertaken a massive and potentially valuable project. However, they have undertaken statistical comparisons using non-matched groups with little reference to their methods. In a large audit, group numbers could reasonably be expected to nullify the effects of individual group variables provided the groups are fundamentally similar. Unfortunately, in this study the only matched variable appears to be gallbladder removal and therefore statistical analysis would seem inappropriate. There is no doubt as to the value of accurate clinical audit. Our primary concern is that, in general, audit data is of insufficient quality to undergo critical comparative analysis.

In the current political climate it has never been more vital that we as surgeons should carefully evaluate the quality of data collection, its analysis and conclusions. Large audit studies will obviously attract attention from lay persons and may be used in determining performance norms. We feel it is important, therefore, that such investigations are not portrayed as controlled clinical trials.

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Cell biology of human vascular smooth muscle

The recent article on human vascular smooth muscle cells (VSMC), and the implications of *in vitro* cellular differences for clinical restenosis, made interesting reading (*Annals*, September 1994, vol 76, p298). This article presented data on cell studies and hypothesised on the implication of *in vitro* VSMC findings on clinical restenosis.

The VSMC has been extensively characterised *in vitro* and *in vivo* over the last two decades, and the mechanisms of its involvement in intimal hyperplasia continue to be elucidated *(1)*. VSMC have a pivotal role in interaction with various growth factors and cells during the formation of intimal hyperplasia. Important as it is, histological data obtained from atherectomy specimens, post-mortem examination and animal studies have shown that VSMC and its production of intimal hyperplasia cannot be equated with restenosis.

Human restenosis is a complex process and arises from a combination of inadequate luminal dilatation, atheromatous plaque collapse or dissection, thrombosis, acute or chronic vasoconstriction and intimal hyperplasia. More recently, vascular remodelling has been proposed as a major mechanism in restenosis *(2)*. The importance of each of these processes is currently under debate in the cardiology literature and it seems unlikely that vessel thickening arising from intimal hyperplasia alone can account for clinical restenosis *(3,4)*. This interesting discussion was ignored in an article which, nevertheless, selected supportive evidence for the role of VSMC in restenosis, from the cardiology literature.

The reasons for the universal clinical failure of successful animal treatments are not fully explained; the differences may, however, be attributable to the multiplicity of mechanisms which give rise to clinical restenosis. This contrasts with the predominance of intimal hyperplasia seen in animal models of restenosis. In addition, treatment dosages which have been effective in animals, cannot be achieved in patients because of the risks of systemic toxicity. Intimal hyperplasia is produced as a continuously evolving process occurring in all patients, rather than a discrete occurrence in some patients only. Measurements used in clinical trials of restenosis may not be sensitive enough to detect the efficacy of treatments which target intimal hyperplasia in the presence of the other factors which contribute to restenosis. Failure of drugs in clinical trials may, therefore, be independent of any fundamental differences in SMC biology *(5)*.

Intimal hyperplasia and vascular remodelling appear to be ubiquitous responses to injury which occur after all vascular interventions. The major factor that determines clinical restenosis may be the adequacy of the post-intervention vascular lumen and its ability to accommodate the reactive response to injury. Angioplasty failure then becomes a consequence of an inadequate post-procedural lumen, possibly from plaque collapse and acute vasoconstriction. The processes involved in producing a poor post-dilatory lumen, such as a resistant plaque, are likely to be encountered on subsequent dilatations, and are likely to be the reasons for increased restenosis rates when angioplasties are performed for restenosis.

Finally, restenosis is the recurrence of a stenosis at the site of a previously treated stenosis. It is incorrect, therefore, to refer to primary vein graft stenoses, or anastomotic stenoses (where there has been no previous stenosis) as restenosis. Intimal hyperplasia is probably more important in graft stenoses than angioplasty restenosis, and the cellular processes described in the article may be more applicable in graft stenosis.

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References

1 Waller BF, Orr CM, Pinkerton CA, Slack JD, Van Tassel JW, Peters T. Balloon angioplasty restenosis: intimal proliferation and chronic elastic recoil. In: Casteneda-Zuniga WR, Tadavarthy SM, eds. *Interven-*