What is already known on this topic

Risk factors associated with postoperative mortality in colorectal cancer surgery are well established

Predictive models are available for surgical patients in general but are not applicable for predicting individual risk and analysis of subgroups in patients with colorectal cancer

What this study adds

A dedicated model has been developed to predict operative mortality for patients undergoing surgery for colorectal cancer

This modified model is presented in a format that is suitable for frontline clinicians

results of treatment between units. However, before such comparative studies can be undertaken it will be essential to ensure inclusion of all patients and to have robust methods of data validation.

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1 Spiegelhalter DJ, Aylin P, Best NG, Evans SJW, Murray GD. Commissioned analysis of surgical performance by using routine data: lessons from Bristol inquiry. *J R Statist Soc A* 2002;165:1-31.
2 The Association of Coloproctology of Great Britain and Ireland Database and Dataset [computer program]. Version 2 for Access 2000. (UK):ClinIT 2000. www.cancernw.org.uk/clinit/products.htm?productindex=1 (accessed 23 Mar 2003).
3 Dripps RD, Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. *JAMA* 1963;178:261-6.
4 Department of Health. Hospital episode statistics, Main operations 2000/01. www.doh.gov.uk/hes/standard_data/available_tables/main_operations/index.html. (accessed 23 Mar 2003).
5 Callum KG, Gray AJG, Hoile RN, Ingram GS, Martin IC, Sherry KM, et al. Appendix A. In: *Then and now: the 2000 report of the national confidential enquiry into perioperative deaths*. London: NCEPOD, 2000:125-6.
6 Turnbull RB Jr, Kyle K, Watson FR, Spratt J. Cancer of the colon: the influence of the no-touch isolation technique on survival rates. *Ann Surg* 1967;166:420-7.
7 Hosmer DW, Lemeshow S. *Applied logistic regression*. 2nd ed. New York: John Wiley, 2000.
8 Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982;143:29-36.
9 Treasure T. Whose lung is it anyway? *Thorax* 2002;57:3-4.
10 Holme T, Johansson H, Cedermark B, Ekelund G, Rutqvist LE. Influence of hospital and surgeon-related factors on outcome after treatment of rectal cancer with or without preoperative radiotherapy. *Br J Surg* 1997;84:657-63.
11 Khuri SF, Daley J, Henderson W, Hur K, Demakis J, Aust JB, et al. The Department of Veterans Affairs' NSQIP: the first national, validated, outcome-based, risk-adjusted, and peer-controlled program for the measurement and enhancement of the quality of surgical care. National VA Surgical Quality Improvement Program. *Ann Surg* 1998;228:491-507.
12 Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg* 1991;78:355-60.
13 Khuri SF, Daley J, Henderson W, Hur K, Gibbs JO, Barbour G, et al. Risk adjustment of the postoperative mortality rate for the comparative assessment of the quality of surgical care: results of the National Veterans Affairs Surgical Risk Study. *J Am Coll Surg* 1997;185:315-27.
14 Copeland GP. Surgical scoring, risk assessment and the surgeon. *J R Coll Surg Edinb* 1992;37:145-8.
15 Sagar PM, Hartley MN, MacFie J, Taylor BA, Copeland GP. Comparison of individual surgeon's performance. Risk-adjusted analysis with POSSUM scoring system. *Dis Col Rectum* 1996;39:654-8.
16 Tekkis PP, Kocher HM, Bentley AJ, Cullen PT, South LM, Trotter GA, et al. Operative mortality rates among surgeons: comparison of POSSUM and p-POSSUM scoring systems in gastrointestinal surgery. *Dis Col Rectum* 2000;43:1528-32.
17 Daley J, Henderson WG, Khuri SF. Risk-adjusted surgical outcomes. *Annu Rev Med* 2001;52:275-87.

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RESEARCH POINTERS

The thrifty phenotype hypothesis and hearing problems

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Shortness indicates that hearing problems in adulthood may be programmed at birth

continued over

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While looking for solutions to sensorineural hearing loss (SNHL) induced by age or noise, a serious incurable health problem, we became interested in the thrifty phenotype hypothesis because diseases related to this hypothesis are sometimes those linked to SNHL.[1] According to the hypothesis, events during fetal life, such as malnutrition, may cause disease in adulthood. The malnourished fetus makes metabolic adaptations, which may become permanently programmed, persisting throughout life and causing disease later in life. For example, cardiovascular disease,[2] hypertension, obesity, and hypercholesterolaemia are related to reduced fetal growth as reflected by a reduced birth size and to SNHL.

The mechanisms behind the thrifty phenotype hypothesis are unclear, but links to insulin-like growth factor I (IGF-I) have been suggested. During development, IGF-I is crucial for several organs. This includes the size of the cochlea and auditory neurones; the innervation of the auditory sensory cells; and the postnatal survival, differentiation, and maturation of auditory ganglion cells.[3] Intrauterine growth retarded newborn babies and malnourished pregnancies have lower concentrations of IGF-I. Also, in Turner syndrome SNHL is associated with short stature and lower concentrations of IGF-I.[4] To test the thrifty phenotype hypothesis on SNHL, we reanalysed data from two previous samples, assuming that people who are short in stature are over-represented among non-syndromic individuals with SNHL.

Participants, methods, and results

We assessed hearing with standard audiometry in 479 men aged 20 to 64, who were exposed to noise in their jobs, and 500 randomly selected 18 year old

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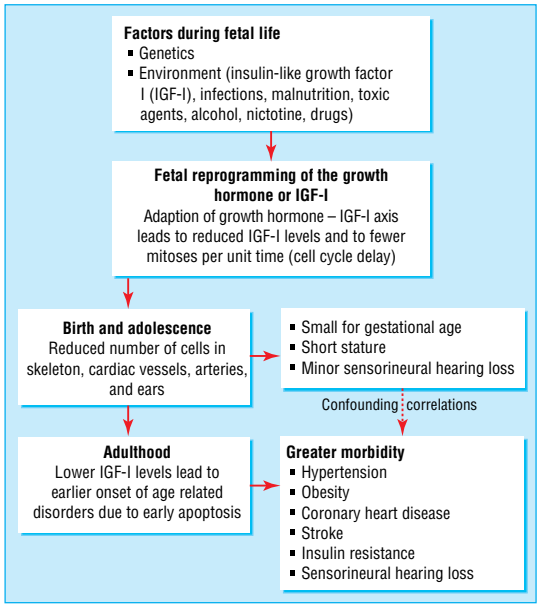
male conscripts born in 1974. We had data on body height, weight, exposure to noise, occurrence of hereditary taint for hearing loss, and other medical disorders including use of drugs.

Among the conscripts, using odds ratios, shortness was found twice as often in those with SNHL as in men with normal hearing. SNHL was also associated with a positive heredity for hearing loss but not with noise exposure. Short workers (less than two standard deviations below the mean) had worse hearing than expected by age (below the 10th centile given in ISO 7029), three times more often than taller workers and were 12 times more often taking drugs. To further test the thrifty phenotype hypothesis on hearing, we used multiple linear regression to model the high frequency hearing thresholds (the average of 3, 4, and 6 kHz bilaterally) among the noise exposed workers as a function of body height (cm), age (years), and hypertension (yes or no). Older short men with hypertension had significantly worse hearing ($P \leq 0.01$), but among tall men, hypertension had no effect on hearing and the influence of age was less pronounced ($R^2 = 0.37$, hypertension and height adding 9%).

Comment

Sensorineural hearing loss (SNHL) in adulthood may be programmed at birth: the thrifty phenotype hypothesis is applicable to SNHL. One mechanism in common to fetal growth retardation, cardiovascular disease, hypertension, and SNHL might be low IGF-I concentrations during fetal life (figure). Indeed, adults with low IGF-I concentrations have features of the metabolic syndrome, a combination of visceral obesity, insulin resistance, dyslipidaemia, and hypertension,[5] and, probably, also SNHL. Since IGF-I is a powerful mitogen, a reduced capacity to maximise the speed of the cell cycle during development comes into focus.[4] Consequences of a reduced number of cell cycles during development are fewer auditory sensory cells, ganglion cells, and neurones at birth and earlier hearing loss symptoms due to apotosis of the auditory sensory cells induced by age or noise.[4] Hypertension and hypercholesterolaemia are commonly believed to cause SNHL; we now consider these confounding superficial markers.



Working hypothesis for sensorineural hearing loss (SNHL) because of fetal events

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1 Hales CN, Barker DJ. Type 2 (non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. *Diabetologia* 1992;35:595-601.
2 Leon DA, Lithell HO, Vagero D, Koupilova I, Mohsen R, Berglund L, et al. Reduced fetal growth rate and increased risk of death from ischaemic heart disease: cohort study of 15 000 Swedish men and women born 1915-29. *BMJ* 1998;317:241-5.
3 Camarero G, Avendano C, Fernandez-Moreno C, Villar A, Contreras J, de Pablo F, et al. Delayed inner ear maturation and neuronal loss in postnatal Igf-I-deficient mice. *J Neurosci* 2001;21:7630-41.
4 Barrenäs M, Landin-Wilhelmsen K, Hanson C. Ear and hearing in relation to genotype and growth in Turner syndrome. *Hear Res* 2000;144:21-8.
5 Bjorntorp P. Neuroendocrine abnormalities in human obesity. *Metabolism* 1995;44(suppl 2):S38-41.

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