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Radiation risk of screening with low dose CT

I read with interest the article by MacRedmond *et al*[1] on screening for lung cancer using low dose CT scanning and the related editorial by Gleeson[2] which provides a comprehensive summary of the benefits and potential pitfalls of such a screening. However, I noticed that, in both articles, the important issue of the potential radiation risks associated with low dose CT screening for lung cancer has not been addressed.

Previously published reports have suggested radiation risks even with a low dose CT scan as part of a regular screening programme[3] and also of a possible synergistic interaction between the risk from smoking and radiation exposure.[4–7] Brenner[3] estimates that, if 50% of all current and former smokers in the US population aged 50–75 years received annual CT screening, the estimated number of lung cancers associated with radiation from screening would be 1.8% (95% credibility interval 0.5% to 5.5%) more than the otherwise expected number. Considering an upper limit of a 5.5% increase in lung cancer risk attributable to annual CT related radiation exposure, he feels that a mortality benefit of considerably more than 5% would be necessary to outweigh the potential risks of radiation. This estimation was derived from cancer incidence data for atomic bomb survivors.[7]

Several other reports[4–6 8] have suggested a link between radiation exposure and lung cancer. Potential radiation risks associated with multiple CT scans should therefore be considered as one of the limiting factors for such screening.

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Dr MacRedmond was asked to comment but no reply who received by the time this issue of *Thorax* went to press.

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Effect of dichotomising age in multivariate model analysis

We read with interest the paper by Soler-Cataluña and colleagues[1] that examined—in an impressive prospective study with 5 years follow up—factors predicting poor prognosis and mortality in patients with severe acute exacerbations of chronic obstructive pulmonary disease (AECOPD). Their findings are complementary with the current available literature in identifying that older age, arterial carbon dioxide tension, and acute exacerbations were independent predictors of mortality in their cohort group.

We have concerns, however, regarding both their analyses and conclusions. Firstly, several studies[2–4] have given advice on the limitations of dichotomising continuous predictors as they come at a cost "as explanatory variables could be seriously misleading, both in respect of which variables are significant in the model, and perhaps also with respect to the overall predictive ability".[2] Soler-Cataluña and colleagues state that in their multivariate model "the frequency of acute exacerbations, age and Charlson index were analysed as categorical variables".[1]

Secondly, and perhaps more importantly, the authors have reported older age (clearly a non-modifiable factor) as a predictor of death. They do not state whether they believe this to be old age per se or an age related potentially modifiable variable. Have the authors collected data on social support, physical disability, depression, quality of life, and any palliative care their patients may have received during the follow up period? These variables may have some effect on mortality in this exclusively male COPD patient cohort. Our own group has recently published data on 1 year mortality following hospitalisation for AECOPD in a slightly older group of subjects (mean age 73 years *v* 71 years in the patients studied by Soler-Cataluña and colleagues) with worse baseline spirometry (mean percentage predicted FEV_1 39%). In our study age was not a mortality predictor on either univariate or multivariate analysis. Quality of life, level of disability, severity of depression, readmission, use of long term oxygen therapy, and duration of original admission (all of which are arguably related to age) were all univariate predictors of 12 month mortality, with only the quality of life score remaining a significant predictor on multivariate analysis.

We wonder whether the inclusion of age related variables in the study by Soler-Cataluña *et al*, together with the use of age as a continuous variable, might have resulted in qualitatively or quantitatively different conclusions regarding the effect of age on prognosis. However, the inclusion of duration of original admission and of frequency of readmission in our own list of predictors[5] would support their suggestion that severe AECOPD could have an adverse impact on longer term mortality.

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Authors' reply

We wish to thank Dr Yohannes for his interest and comments on our study[1] and have the following comments on the questions he raises.

Firstly, although it is true that in some cases the transformation of continuous variables into dichotomised variables my induce some changes in the results obtained, in other cases the use of continuous data may conceal some partial effect, particularly if the predictive relation is non-linear. In fact, in our study the only age group to show a poorer prognosis were those aged ⩾75 years (odds ratio (OR) 5.26, 95% CI 2.70 to 10.24). In the same way, categorisation of the number of exacerbations allowed us to review the differential effect of repeated exacerbations. For these reasons, and in order to make interpretation of the results easier, we

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decided to apply categorisation of some continuous variables in our study. On the other hand, we should mention that this transformation of variables did not modify the results, as both age and the number of exacerbations behaved as independent prognostic factors on inclusion in the model as continuous variables. Specifically, in this predictive equation, age proved to be an independent prognostic variable with an OR of 1.06 (95% CI 1.01 to 1.11). The same applies to the number of exacerbations with an OR of 1.20 (95% CI 1.03 to 1.39).

Secondly, with regard to the role of age as a predictor of mortality, different studies involving both stable patients[2] and acute cases[3 4] have also found age to be an adverse prognostic factor. Despite such evidence, we consider the hypothesis suggested by Yohannes—that other age related and potentially modifiable variables would determine the prognostic effect attributed to age—to be very interesting. Unfortunately, in our analysis we did not include measures such as social support, physical disability, depression, or quality of life so we are unable to assess their specific weight. Almagro *et al*,[5] in a study that also explored mortality predictors after hospitalisation and which considered variables of this kind, found age to have a predictive value in the univariate analysis, but this effect disappeared in the multivariate study. Therefore, as suggested by Yohannes, it is probable that the effect of age may be minimised when other predictors that condition or define such an effect are included in the model.

In conclusion, age dichotomisation did not substantially change the results and conclusions drawn in our study. Re-analysis of the data using continuous (non-dichotomised) variables continues to suggest that severe exacerbations are independent predictors of mortality.

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Diaphragm paralysis after nephrectomy

We read with interest the case report by Moore *et al*[1] on the diaphragm weakness of two patients after anatomically distant surgery.

We are currently following a patient who had bilateral paralysis of the diaphragm after a nephrectomy for renal cancer. The patient, a 60 year old male non-smoker without any concomitant cardiac or lung disease, underwent surgery in August 2004 and immediately after the operation he complained of orthopnoea. Chest radiographs showed the elevation of both hemidiaphragms, which was not present preoperatively, along with a restrictive ventilatory defect detected by spirometry (TLC 61% predicted, VC 72% predicted, FEV_1 67% predicted, FEV_1/VC 70%). The diagnosis of bilateral paralysis was confirmed by electromyography and respiratory muscle strength assessment in October 2004. Because of a nocturnal oxygen desaturation, he started with nightly non-invasive ventilation. Up to now he has also undergone periodic courses of respiratory muscle training. In 2004 and 2005 he was checked regularly and an improvement in VC was found, but not in Pımax nor in TwPdi. Moreover, at the December 2005 check up the nocturnal oxygen desaturation had significantly improved and the patient had stopped the ventilation support.

Diaphragm paralysis is associated with renal cancer and is considered to be a paraneoplastic syndrome.[2 3] In our patient, however, the temporal link between the surgical operation and paralysis is evident. Moreover, during the operation and after the perioperative period our patient did not undergo central venous cannulation, nor did he experience any electrolyte disturbance. Postoperatively, the patient also underwent magnetic resonance imaging which excluded any injury to his spinal cord. The similarity between the case histories presented by Moore *et al*[1] and our patient therefore appears to be evident.

In addition, we think the patient's follow up is of interest. So far, the patient's VC has recovered 0.48 l, being 4.2 l and 86% of predicted value in orthostatism. Furthermore, VC now accounts for 2.3 l and 47% of predicted in clinostatism and can assure a normal oxygen saturation during sleep. However, the patient's diaphragm is still paralysed, since the TwPdi value is extremely low (3 cm H_2O) and the fall in VC from orthostatism to clinostatism is significant (45%). The recovery in VC might be due only to the increase in strength of the accessory inspiratory muscles, probably due to the respiratory muscle training courses. This finding further supports the recommendation by Moore *et al*[1] to measure the diaphragm strength separately from global inspiratory muscle strength in patients with raised hemidiaphragms after surgery.

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