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Follow-up regimen after lung cancer treatment: about the how and why

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Lung cancer is the leading cause of cancer-related mortality worldwide and even after surgery with curative intent, recurrent disease is found in up to 30% of patients (1). For this reason, treated lung cancer patients are followed by anamnesis, physical examination and chest computed tomography (CT) scans regularly. Usually, patients are closely followed during the first five years after treatment, although no widely accepted follow-up regimen exists regarding the frequency of visits and the type of additional imaging examinations.

To define an optimal follow-up scheme, it's important to define our aim. In general, follow-up examinations after curative lung cancer treatment have three major aims. First, mainly shortly after the treatment, a physician wants to check the direct result of treatment in terms of physical recovery. Second, a physician wants to give psychosocial support or refer to a psychosocial specialist, if indicated. The third aim, which gets increasingly important on the longer term after finishing treatment, is to detect recurrent disease or second primary lung cancers at an early stage, preferably when curative treatment is still an option. And of course, we would like to offer this follow-up in a cost-effective way, given the high pressure on healthcare systems, high costs and potential harms of overdiagnosis.

Currently, there is debate on whether this follow-up after

treatment with (bi)-annual CT scans and accompanying hospital visits is beneficial for the patient. Westeel *et al.* recently published the results of a large randomized-controlled trial including lung cancer patients in 122 hospitals and tertiary centres in France between 2005 and 2012, aiming to compare follow-up after lung cancer treatment with either thoracoabdominal CT scans or chest X-rays (2). They randomized 1,775 patients to receive either CT-based follow-up or minimal follow-up (only chest X-ray and hospital visit) twice a year in the first two years after surgery for lung cancer and annually for the next three years. The main findings were a lack of overall survival difference between the groups after a median follow-up time of 7.2 years [8.5 years (95% CI: 7.4–9.6) in the minimal follow-up group *vs.* 10.3 years (95% CI: 8.1–not reached) in the CT-based follow-up group; adjusted hazard ratio (HR) 0.95, 95% CI: 0.83–1.10], as well as the lack of difference in disease-free survival. However, in the CT-based follow-up group they did find more cases of early recurrence and second primary lung cancer [329 (37.1%) *vs.* 273 (30.7%)] in the minimal follow-up group. Since these early diagnoses are more amenable to curative-intent treatment, they concluded that the use of CT-based follow-up is still supported, especially in countries where lung cancer screening is already implemented, alongside

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with other supportive measures (2). Whether newer CT techniques and lung nodule management strategies involving volume-based measurements, which are regarded to be more precise and better able to detect growth already at smaller lung nodule size, would benefit the CT-based follow-up results is still unknown (3,4).

The same topic, enhanced with a cost-effectiveness analysis, was investigated by Rodríguez-Cano and colleagues in a single-centre retrospective analysis (5). They studied 392 consecutive patients who underwent surgery for lung cancer, collecting and analysing clinical data and tests performed during follow-up after surgery. Overall median follow-up time for all patients was not stated, although patients with stage I disease had longer median follow-up time and better median overall survival than patients treated for stage III lung cancer [46.2 months (interquartile range, 41.9–50.5) *vs.* 28.5 months (interquartile range, 23.2–33.3) and 128.0 months (interquartile range, 72.4–183.6) *vs.* 52.0 months (interquartile range, 44.4–59.6), respectively]. The authors compared effectiveness of different follow-up strategies, expressed as relevant and irrelevant consultations. Here, a relevant consultation was the one where a relapse of disease was detected resulting in change of follow-up and/or treatment of the patient.

Not strikingly, profitability (in terms of lung cancer diagnosis) of tests such as a CT scan was much higher in unscheduled hospital visits with patients presenting earlier than planned due to symptoms such as pain or haemoptysis, when compared to regular scheduled follow-up visits. The highest profitability rate for a CT scan during scheduled visits was found for patients treated for stage III lung cancer [48/480 CT scans (10.0%) *vs.* 48/966 CT scans (5.0%) for patients treated for stage I and 32/457 (7.0%) CT scans for stage II disease]. The latter is in line with expectations as well, as recurrent disease is more often found in later stages (6).

One thing to conclude from the study of Rodríguez-Cano *et al.* (5) is that laboratory tests should not be part of regular scheduled follow-up visits after surgery for lung cancer. Indeed, frequently used guidelines for follow-up of non-small cell lung cancer after curative resection do not include blood test in their follow-up advice (6-8).

Results of previous lung cancer screening trials, such as the randomized-controlled National Lung Screening Trial, showed that only chest CT scans and not chest X-rays can assist in early lung cancer detection and mortality reduction in high-risk populations (9). Lung cancer patients who

are followed-up after curative treatment are at high-risk of develop a second primary lung cancer by definition, since they already showed to be prone to develop the disease (10,11). This indicates that CT scans should be the examination of choice in the follow-up of lung cancer patients, to be able to detect second primary lung cancer at an early, treatable, stage.

Given the results of Rodríguez-Cano *et al.*, should we now change our CT-based follow-up regimen after curative surgery for lung cancer? We do not think so. However, we do see the value of fast-track consultation routes for additional unscheduled visits for patients with clinical complaints after treatment, despite the fact that these symptomatic patients are expected to be diagnosed more often in later cancer stages compared to malignancies diagnosed during scheduled visits. So, whether or not this increased profitability of examinations in unscheduled visits will eventually lead to better patient outcomes in terms of survival remains to be seen. For that reason, we have to carefully evaluate the benefits of follow-up tests.

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