Follow up after primary treatment: curable diseases primarily treated with surgery

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Introduction

There is considerable debate at the present time concerning the role and relevance of follow-up following primary surgical treatment with curative intent in patients presenting with cancer. There are many factors which govern the aims of follow-up programmes and also the determinants of success of individualised follow-up. Clearly different tumour types have different levels of aggressiveness and will therefore have differing disease-free interval and survival figures. Even if one looks at individual cancer types, taking breast cancer as an example, prognosis will depend on many factors such as grade, stage and size of tumour. The primary aim of follow-up is to detect at an early stage either local or systemic recurrence of the primary tumour. The second aim of follow-up is to detect new primary cancers of the contralateral side or in specific cancers to look for other cancer types which occur more commonly in patients who were diagnosed with specific primary cancers. In certain instances follow-up is also designed to look for complications after primary treatment and finally there is a body of opinion to suggest that follow-up is of benefit in the management of psychological problems which occur in patients with a diagnosis of cancer.

The real issue at stake when developing protocols for follow-up is an assessment of the determinants of success. Foremost is the extent to which follow-up programmes will detect either local or systemic recurrence. Furthermore, the issue relates to whether such recurrences are detected at the time of the visit to the follow-up clinic or in fact are found by the patient who is then referred by the GP to the follow-up clinic with a suspected recurrence. This raises the important point of the cost of follow-up. The cost effectiveness of follow-up in cancer is very difficult to determine as it is almost impossible to match cost of follow-up with the increased number of years of survival in each case. Finally it makes sense to match the frequency of follow-up with the risk of recurrent disease — the greater the risk of recurrence then the greater should be the frequency of follow-up. In determining protocols therefore, it seems logical that each patient should be individualised, or each risk category of every cancer should be categorised, according to risk of recurrence. One obvious example of this would be whether follow-up of patients with ductal carcinoma in situ of the breast should be different from those with invasive adenocarcinoma of the breast. Whilst it seems logical to follow this schedule, there are major practical difficulties in individualising follow-up programmes according to levels of risk. Therefore, in deciding on frequency of follow-up there must be a balance between determining risk of recurrence and also deciding what type of follow-up programme is manageable and easy to follow in individual units.

The following therefore, is the current evidence base regarding follow-up in the relevant cancers where primary surgical treatment is the mainstay of management. A good example of the problems relating to follow-up relates to controversies in the follow-up of patients with breast cancer. Therefore breast cancer is used as an example of the pros and cons of follow up programmes and other cancers are mentioned briefly although the same principals apply to other cancers as they do to breast cancer.

Breast cancer

Routine follow-up in specialist surgical or oncology clinics after completion of primary treatment for breast cancer is standard practice in most countries. There is considerable uncertainty about the optimum method of follow-up for women with breast cancer in remission [1].

Follow-up visits in the UK usually last up to 10 years despite many controversies about the benefits of this practice [2]. In a survey of all Consultant General Surgeons with a response rate of 61% it was found
that 90% considered follow-up worthwhile, although many commented that the major value was for the psychological benefit to patients rather than for oncological reasons. 29% would follow-up their patients for 1–5 years, 27% for 5–10 years, and 33% for 10 years or for life. The majority (69%) did no follow-up investigations on asymptomatic patients (excluding mammography) and 29% indicated that they did. The frequency of mammograms varied from 2–3 years [3].

The majority of women who experience recurrence do so between regularly scheduled follow-up appointments by finding it themselves [4,5] and are more likely to see their GP than have the recurrence diagnosed at a specialist clinic [6].

In a randomised controlled trial (RCT) comparing routine hospital follow-up with GP follow-up for women with breast cancer in remission, those women randomised to hospital follow-up were interviewed about their experience. Access to cancer expertise and diagnostic tests were valued particularly in the early stages of follow-up. Seeing the same doctor was also important as women felt there was knowledge of the individual case. However some women felt seeing different doctors was advantageous as it provided a second opinion and limited the exposure to staff in whom patients lack confidence or simply dislike. Women felt that there was a lack of time in hospital appointments to gain the information they wanted. The data suggest that continuity of care and access to specialist care is important in the earlier stages of follow-up, whereas the need for an unrushed consultation persists over time [7].

In an earlier RCT [8] involving 296 women, routine follow-up of breast cancer in primary care over 18 months compared hospital with GP follow-up, was not associated with an increase in time to diagnosis, increase in anxiety or deterioration in health related quality of life. Most recurrences 69% (18 of 26) in this study presented as interval events and 44% (7 of 16) of the recurrences in the hospital group presented first to the GP. Therefore the majority of recurrences present to the GP irrespective of continuing hospital follow-up. As these two methods of health delivery show no significant difference in the primary clinical outcomes, patient satisfaction with follow-up was considered as a secondary outcome of the RCT. The GP group reported greater satisfaction with follow-up than the hospital group.

Recommendations are made that the patients should be offered a choice of follow-up between their GP and hospital with complete and accurate information about the goals, expectations, and limitations of the follow-up programme [8].

The main purpose of follow-up is the earliest possible diagnosis of a relapse with a view to applying a curative second-line treatment. As distant metastatic disease is currently incurable, local recurrence and a contralateral breast cancer are the relapses that might be detected at a routine follow-up visit that are potentially curable. Two RCTs have shown that adding routine chest X-ray, bone and liver scanning to clinical surveillance does not improve survival [9] and this has also been shown in a study assessing intensive (annual mammograms, biannual chest X-ray and bone scan versus clinical (c/e and mammogram) follow-up at 10 years [10]. Mammography is the only diagnostic test of established value although the optimum frequency is not yet defined [11].

Some women may feel reassured after a follow-up visit even if they find the days before it stressful, but the reassurance may be unfounded given that routine follow-up has not been shown to improve survival. Whereas some women may find that routine hospital visits remind them of their disease and are a source of continuing anxiety. Hospital specialist nurse-led follow-up clinics are an option which would provide access to expertise as well as psychological support. Based on the studies reported an option could be to provide access to a specialist hospital clinic in the first couple of years post initial treatment, and then transfer to the GP but with open access to the specialist clinic thus allowing more time for women with problems and less inconvenience and anxiety of returning to the hospital regularly.

Recent suggestions by the NHS Clinical Outcomes Group recommend that follow-up of breast cancer patients in hospital should be minimised-ordered guidelines. The cost benefit aspects of regular examinations in cancer patients have been discussed but no general consensus on a protocol has been reached [12].

Recommendations for breast cancer follow-up would therefore include history taking and physical examination every six months for the first three years after primary treatment and then yearly after that. Contralateral mammography should be performed each year and patients with breast conserving surgery should have their first post treatment mammogram six months after completion of radiotherapy. Examinations such as pelvic ultrasound, chest X-ray, bone scan, ultrasound of the liver and tumour markers are not justifiable outside of clinical trials.

**Lung cancer**

Lung cancer is chosen here as a special example relating not just to the risk of local recurrence but the
risk of developing a second lung cancer. After primary treatment of the cancer, the rate of developing a second primary cancer is 1–5% per patient per year for both non-small cell and small cell lung cancer. Several follow-up guidelines have been published for lung cancer including medical history taking, physical exam, tumour markers, chest X-ray, abdominal CT scans and bronchoscopy. Unfortunately there is no proof that these guidelines, which are intensive high cost strategies, increase the survival or indeed the quality of life in these patients. This is because these follow-up programmes detect only a minority of patients with curable recurrences. The State of the Art project, which is run by the European School of Oncology, suggests that a chest X-ray every six months for the first few years followed by yearly chest X-rays should be carried out for non-small cell lung cancers. For small cell lung cancers chest X-rays every two to three months for three years and then every six months for a period of five years followed by yearly chest X-rays should be carried out. Clearly separate symptoms need to be looked upon on an individual basis.

Colon cancer

The rules of follow-up strategies in colon cancer as in other types of cancer are to detect recurrent disease with potential curative intent and also to detect new primary lesions. It is well established that approximately 30% of patients with colon cancer treated by curative intent will develop recurrent disease. Most studies indicate that an intensive follow-up programme should be carried out with a physical examination and determination of carcinoma-embryonic antigen every three to six months for three years and then every six to twelve months thereafter for five years. Colonoscopy and chest X-ray should be carried out annually. The real debate in colonic cancer concerns the intensity of follow-up. Some studies have demonstrated that an intensive follow-up programme might be cost effective especially those presenting with hepatic metastasis. Meta-analyses performed in studies relating to this problem have shown that an intensive follow-up programme detected more recurrent tumours amenable to curative resection. This is however by no means proven and other studies have failed to demonstrate a cost–benefit ratio where routine use of follow-up is carried out in patients with colorectal cancer. The recommended guidelines of the American Society of Clinical Oncologists are that patients should be examined every three to six months for the first three years and then annually subsequently [13]. A yearly chest X-ray and colonoscopy every three to five years should be done while CEA every three months in patients with stage two or three disease for two years after surgery should be done. The use of this tumour marker is performed mainly to detect liver metastasis.

Germ cell tumours

One final example of the value of follow up is in germ cell tumours which are curable even in advanced stages [14,15]. In men with a stage I non-seminoma testicular cancer there is a relapse rate of 30% and the median time to relapse is five to six months. In these patients 50% will relapse in the retroperitoneal space and two thirds of patients will have raised tumour markers. Most protocols suggest monthly physical examination, chest X-ray and serum tumour markers with abdominal CT scan every three months in the first year after primary surgical treatment. Later recurrences have been reported and these patients should, for this reason, be followed life long. In men with stage I and stage II seminomas up to 50% of patients have recurrences which depend on the staging and primary treatment. As recurrent disease is curable with further treatment, then a follow-up programme is of benefit in these patients and has been shown to be cost effective. These patients should have a similar follow-up programme as above.

References