J R Coll Physicians Edinb 2015 45: 206–8
http://dx.doi.org/10.4997/JRCPE.2015.306

Utility and prevalence of imaging for underlying cancer in unprovoked pulmonary embolism

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ABSTRACT
Current guidelines state that patients over 40 years of age with a first unprovoked pulmonary embolism should be offered limited screening for possible cancer and considered for intensive screening (abdomino-pelvic computed tomography and mammography), despite no evidence for the latter. The aim of this study was to evaluate the clinical utility and cost of intensive screening in routine clinical practice.
Methods All patients diagnosed with a first unprovoked pulmonary embolism between January 2014 and June 2014 in a single large UK teaching hospital were included. The information management department searched for patients with an International Classification of Diseases 10 discharge diagnosis of pulmonary embolism and limited to 'acute pulmonary embolism with/without cor pulmonale'. Only patients with unprovoked pulmonary embolism were included. Patients with chronic medical conditions predisposing to pulmonary embolism were excluded. NHS costs were obtained from the Trust Finance Department. These costs were used to generate the costs of limited versus intensive screening, and then scaled up using adult population census information and assuming the same incidence of idiopathic pulmonary embolism to estimate the annual NHS cost of intensive screening.
Results Ninety-two patients were diagnosed with pulmonary embolism, and 25 met the inclusion criteria. Clinical examination was often incomplete (84%). Limited screening was often missed (urinalysis 100%, serum calcium 64%). Intensive screening was performed in the majority of cases (68%, all abdomino-pelvic computed tomography with no cancer detected) with an £88 excess cost per patient.
Conclusion Intensive screening in first unprovoked pulmonary embolism has a low yield, is costly and should not replace thorough clinical examination and basic screening.

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KEYWORDS computed tomography, cost effectiveness, guidelines, screening, malignancy, pulmonary embolism

DECLARATION OF INTERESTS No conflict of interest declared

INTRODUCTION

The association between venous thromboembolism and cancer has been documented by a number of studies.[1-3] The question of whether to search and how to search for underlying cancer when venous thromboembolism is diagnosed has been the subject of considerable opinion in the literature.[4-8] To date, there is no conclusive evidence that extensive screening for cancer in this scenario improves mortality and there is a lack of large randomised trials to clarify this issue.[4,5]

It is common clinical practice to perform baseline investigations in order to search for occult malignancy in the setting of unprovoked venous thromboembolism, including blood tests and ultrasound imaging, bearing in mind the need to avoid excessive testing to avoid unnecessary patient anxiety. Ultrasound avoids radiation exposure; indeed, computed tomography of the abdomen requires radiation exposure equivalent to 400 chest radiographs or 3.3 years of background radiation,[9] and can also lead to unnecessary detection of irrelevant findings leading to further patient anxiety and a vicious cycle of unnecessary investigation.

In 2012, the National Institute for Health and Care Excellence (NICE) published guidelines on the management of venous thromboembolic disease and investigations for cancer.[10] These advise offering all patients diagnosed with unprovoked deep venous thrombosis (DVT) or pulmonary embolism (PE), who are not already known to have cancer, the following investigations for cancer: a physical examination (guided by the patient's full history), plain chest radiography, full blood count (FBC), serum calcium, liver function tests

(LFTs) and urinalysis. The guidelines further advise considering further investigations for cancer with an abdomino-pelvic CT (CTAP), plus mammography for women, in patients aged over 40 years with a first unprovoked DVT or PE who do not have signs or symptoms of cancer based on initial investigation. Since publication of this guidance, there seems to have been a shift in clinical practice towards performing CTAP, although the guidance for this is weak. This retrospective study evaluated the clinical utility and financial cost of intensive screening (CTAP and mammography) in patients with a first unprovoked PE.

METHODS

Study population and patient selection

This study was performed at Southmead Hospital (a UK university teaching hospital in south-west England with a catchment area of 500,000). All patients diagnosed with a first unprovoked PE between January 2014 and June 2014 were included. Patients with acute PE were identified by the information management department, who searched for patients with an International Classification of Diseases 10 diagnosis of PE and limited to 'acute PE with/without cor pulmonale' on discharge. Only those with a first unprovoked PE were included in the analysis; those with an underlying medical problem predisposing them to thromboembolism were excluded.

Outcome measures

Notes, investigations, radiology reports and results were reviewed and analysed retrospectively by a single researcher (RH). In order to compare costs of limited versus intensive screening, the Trust Finance Department was consulted for current investigation costs, and then costs were scaled up to population level, using adult population census information and assuming the same incidence of idiopathic PE across the UK to calculate the annual UK financial cost of intensive screening. NHS costs used were as follows: Full blood count £4, bone profile (including calcium)/LFT £5, urea and electrolytes £2, urine microscopy £5, abdominopelvic computed tomography £141.

RESULTS

Ninety-two patients were identified during the study period with a PE; of these, 25/92 (27%) had a first unprovoked PE, 16 were male, 9 were female, and the mean age was 65 years (range 30–96).

Basic screening

Rates for each component of both basic and extended screening are given in Table 1. While all patients underwent a history and clinical examination, few had breast or scrotal examination. All patients underwent chest radiography which was normal in 12 patients, with evidence of either atelectasis or small effusion in the remainder but no cancer. Full blood counts were performed in all, and all but one was normal. The abnormal FBC consisted of a microcytic anaemia, which was not followed up or acted on.

TABLE 1 Number and percentage of patients positive or negative for the study criteria (n=25 unless otherwise noted)

Study criterion	No. of patients (%)
Clinical examination	25 (100)
Breast examination	3 (33) (n=9)
Scrotal examination	1 (6) (n=16)
Chest radiography	25 (100)
Full blood count	25 (100)*
Serum calcium	9 (36)**
Liver function tests	24 (96)**
Urinalysis	0 (0)
Abdomino-pelvic CT	17 (68)
Mammography	0 (0) (n=9)
Cancer detected by abdomino-pelvic CT	0 (0) (n=17)

*One abnormal, not followed up **all normal

Extended screening

Seventeen (68%) underwent CT of the abdomen and pelvis and all of these were negative for cancer. There was one incidental benign adrenal adenoma identified of no consequence. The total cost of the 17 CT examinations as per the in-house finance department was £2,397, which equates to a total of £96 per patient if spread over all 25 patients. In contrast a total of just £205, or £8 per patient, would have been spent to complete the outstanding baseline investigations. This equates to an excess cost of £88 per patient for extended screening over and above full basic screening. Two patients were under the age of 40; below the age cut-off noted in the guidance for investigation of first PE for cancer. None of the female patients underwent mammography. In this hospital, baseline screening investigation costs are calculated at £16 per patient, but with additional CT of the abdomen and pelvis this increases to £157 (this excludes the initial chest radiograph and CT pulmonary angiogram used to diagnose PE). While there are no reliable data on the incidence of idiopathic PE, our local incidence rate for first unprovoked PE derived from the data in this survey is approximately 50 per 500,000 adults or 100 per 1 million adults per year. Assuming a similar incidence for the adult UK population of 48 million (2011 census[11]) this equates to 4,800 patients with idiopathic PE on a national level per year. Assuming a similar clinical approach, a total of £422,400 excess costs would be incurred per year.

DISCUSSION

No underlying cancer was detected either by limited or extensive screening in this study which was limited by

low numbers; most patients with PE had known provoking factors. A further limitation of this study is a failure to follow it with an intervention and demonstrate an improvement as a quality improvement study, and relying on case records which may not allow complete capture of a patient episode. For example, we cannot exclude the possibility that urinalysis was perfomed, but not entered in the notes. We also acknowledge we have made some assumptions in the extrapolation of our data to NHS cost in the UK, but the purpose of our study was to illustrate the importance of this potential financial waste and lack of utility of intensive screening, especially CTAP. We therefore feel this is an important (albeit small) study relevant to clinical practice to inform on cost-effectiveness and value of investigations in this scenario. Limited screening for detection of cancer in unprovoked PE is considered to be the most cost-effective approach, yet baseline tests and physical examination were incomplete.

Lack of breast and scrotal examination was noted in addition to calcium testing and urinalysis. While lack of a chaperone or documentation (a not uncommon problem[12]) might explain some of these missing data, given the high number of deficiencies we strongly suspect these were not done because of lack of clinical rigour. One abnormal FBC showing microcytic anaemia was not investigated further. In contrast, with regard to extensive screening, the majority of patients had CTAP performed, although NICE guidance suggests this should be considered rather than always carried out. Guidance also suggests that extensive screening is carried out in the above 40 year age group, and both the patients in this study aged below 40 underwent CT scanning. Guidance for performing mammography is equal to that for CT. However, mammography was not offered to any of the nine female patients. Overuse of CT has implications of monetary cost, opportunity cost for radiology departments, as well as the radiation burden for patients. In this small study, CT of the abdomen and pelvis showed no apparent benefit but raised the potential for psychological morbidity due to excessive investigation. Future randomised studies of adequate power should also assess cost-utility and effectiveness of CTAP and mammography in unprovoked PE as well as the effects on the psychological wellbeing of patients.

In summary, there is some evidence of an apparent shift to CTAP following NICE guidelines[10] in patients with unprovoked PE, while baseline investigations are often incomplete. This has significant potential cost, resource, radiation and psychological implications. Clinical acumen will remain paramount in deciding whom to refer for more extensive screening until clarity is obtained from adequately powered randomised and cost utility studies. Indeed, a further multi-centre review is suggested to further ascertain the number of patients required to scan to detect a malignancy in these cases, which will better inform clinicians as to the utility of this approach. In the interim, clinicians must complete a thorough clinical history, examination and baseline tests – such an approach will at the least allow better targeting of follow up tests and may obviate the need for more extensive testing.

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