

Implementation of NICE recommendations on abdomino-pelvic CT, following unprovoked venous thromboembolism, in a UK teaching hospital: no additional detection of occult malignancy and high numbers of incidental findings

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Abstract

Introduction: NICE Clinical Guideline 144 recommends that patients with an unprovoked VTE, who do not have signs or symptoms of cancer on initial investigation, be considered for further investigation with an abdomino-pelvic CT to exclude occult malignancy. This study aimed to evaluate numbers of scans performed in a UK teaching hospital and outcomes, following this recommendation.

Methods: Retrospective review of CT scans performed before and after publication of the NICE guidance in 2012. CT reports and case notes were analysed. Type and stage of malignancy, treatment and other relevant findings were documented. For the 2014 data set, all incidental radiological findings and follow-up recommendations were reviewed.

Results: The annual number of CT scans requested for “unprovoked VTE”, rose by 142% following publication of NICE Clinical Guideline 144. In the 2011–2012 data set, 21 patients were included, one of which was found to have a malignancy, which was clinically overt at the time of diagnosis i.e. not occult. Five patients (23.8%) had incidental findings requiring further investigation. In the 2014–2015 data set, 51 patients were included, five (9.8%) of which were found to have malignancy. In retrospect, all showed signs/symptoms of potential malignancy on initial investigation. No occult malignancies were detected in the patients correctly referred. Incidental findings warranting further investigation were reported in ten cases (19.6%). On review, follow-up advice was deemed incorrect in four of these.

Conclusion: Addition of an abdomino-pelvic CT scan in patients with a first unprovoked VTE and no signs or symptoms of cancer on initial investigation, significantly increased the number of scans and incidental findings, but did not pick up any additional occult malignancies.

Key points

- The number of CT requests for occult malignancy following unprovoked VTE increased by 142% in our trust following the publication of NICE Clinical Guideline 144
- This did not lead to any additional detection of occult malignancy, but did lead to a large increase in the number of incidental findings, many of which required further investigation and follow-up, with implications for patient anxiety, radiation risk and resources
- Focusing on a thorough history and examination, supported by abnormal baseline investigations would have allowed us to pick up all the patients in whom malignancy was subsequently identified.

Introduction

Unprovoked venous thromboembolism (VTE) comprises a deep vein thrombosis or pulmonary embolism in a patient with:

- no antecedent (within 3 months) major clinical risk factor for VTE e.g. surgery, trauma, significant immobility (bedbound, unable to walk unaided or likely to spend a substantial proportion of the day in bed or in a chair), pregnancy or puerperium, who is not having hormonal therapy (oral contraceptive or hormone replacement therapy) or

- active cancer, thrombophilia or a family history of VTE (because these are underlying risks that remain constant in the patient)¹

The association of cancer with VTE is well recognised. Unprovoked VTE may be the earliest sign of cancer,^{2, 3} with a prevalence of 10% at 12 months.⁴ In view of this, NICE guidance (CG144), published in June 2012, recommends that all patients with an unprovoked VTE, not already known to have cancer, should be investigated with a full history, clinical examination, and routine investigations.¹ These include a chest X-ray (CXR), routine blood

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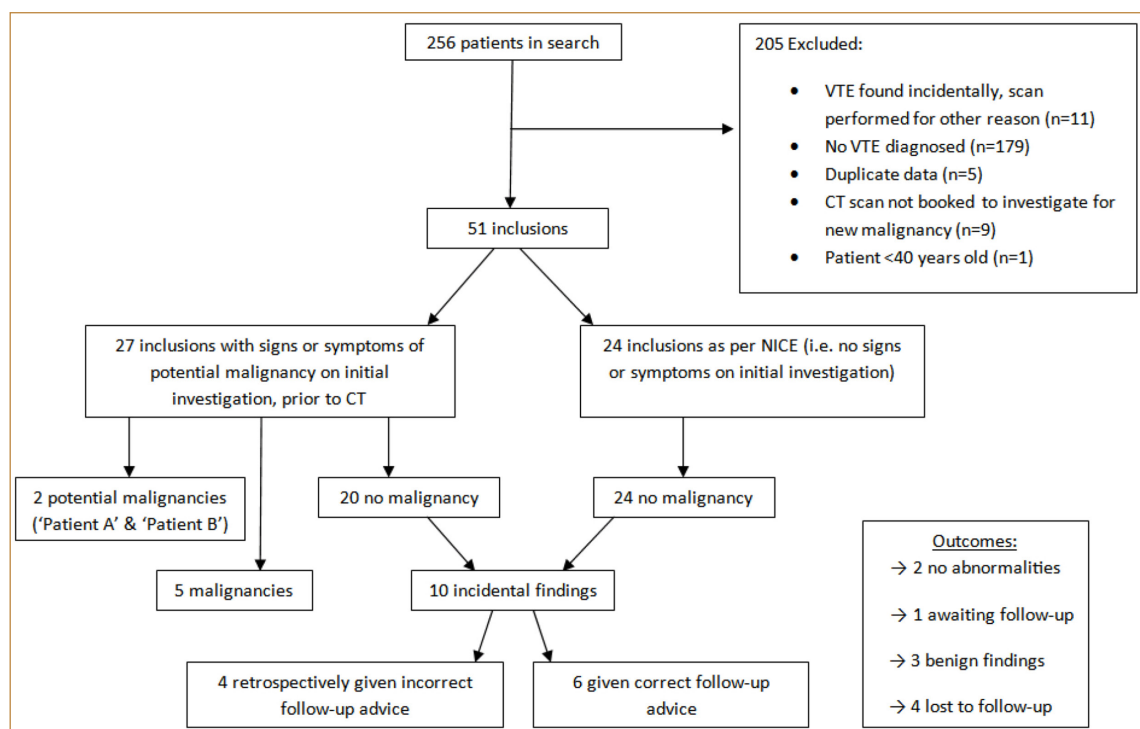


Fig 1. Inclusion flow chart of the 2014-2015 data set

tests (full blood count (FBC), calcium (Ca²⁺), and liver function tests (LFTs)) and a urinalysis. The guideline then goes on to recommend that those patients over 40 years of age who have no signs or symptoms of cancer based on initial investigation should be considered for an abdomino-pelvic CT scan and a mammogram, if female.

The aim of this study was to evaluate the implementation of this guidance in our Trust, as well as the outcome of CT scans performed in patients with unprovoked VTE. Primarily, we hypothesised that there would have been a significant increase in number of patients being scanned for unprovoked VTE post-2012 NICE guidance. Secondly, we hypothesised that this would result in more cancers being detected at an earlier stage; and finally, that this would increase the number of incidental findings and lead to further, possibly unnecessary, investigations.

Methods

A retrospective review was performed of all CT scans requested for unprovoked VTE, performed at The Royal Liverpool University Hospital, a large tertiary teaching hospital, during two time periods, before and after NICE guidance publication in 2012. The first period was from January 2011 – January 2012, the second was from January 2014 – January 2015. A search of the Radiology Information System was performed using the following key words in CT requests: “unprovoked DVT”, “unprovoked PE”, “DVT”, “recurrent DVT”, “recurrent

PE”, “unexplained PE”, “unexplained DVT”, “unexplained VTE” and “underlying malignancy”.

The request forms were assessed for the following inclusion criteria, as defined by NICE guidance:

1. Patient over 40 years old
2. Presenting with unprovoked VTE
3. Having a CT abdomen/pelvis to investigate for underlying malignancy

The CT reports were then analysed and grouped according to whether a malignancy (or potential malignancy) was identified or not. Type and stage of malignancy, treatment and any other significant findings were documented, following case note review. In addition, patients were sub-grouped into those that did not have signs/symptoms of potential malignancy on initial investigation prior to the CT scan (in accordance with the guideline) and those that did. For the 2014 data set, all incidental radiological findings and follow-up recommendations were reviewed by a consultant radiologist (EJ) to retrospectively assess their outcome and relevance where possible. For any equivocal interpretation or follow-up recommendation, the opinion of a sub-specialty expert radiologist was sought.

Results

Between the two time periods (2011–2012 and 2014–2015), the number of CT scans booked to detect malignancy in an unprovoked VTE rose by 142% – from 21 patients in 2011–2012, to 51 in 2014–2015. This confirmed our primary hypothesis. The

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Table I. Malignancies (and potential malignancies) identified in 2014-2015 data set

Age	Presentation	Diagnosis	Treatment
68	DVT, weight loss	Adenocarcinoma of the sigmoid T2N0M0	Sigmoid resection
53 (deceased)	DVT, weight loss, change in bowel habit and deranged LFTs	Widespread metastatic adenocarcinoma, primary unknown	Palliation
55	DVT, weight loss and abnormal CXR	Lymphnode metastatic adenocarcinoma of prostate	Hormone therapy
78 (deceased)	Two DVTs within 2 months' of each other (separate legs), previous bladder cancer	Squamous cell carcinoma in para-aortic lymph nodes, primary unknown	Palliation
75	DVT, weight loss	Primary pancreatic adenocarcinoma T2N0M0	Palliative chemotherapy; not fit for surgery
80 (Patient A)	DVT, weight loss, anaemia	Complex renal cyst	See text
65 (Patient B)	DVT, anaemia	Enlarged perigastric nodes - Ulcerative Colitis (UC) diagnosed	UC treated with oral 5-ASA therapy

initial 2011-2012 search returned 99 cases. In the 21 included, one malignancy was detected. However, in retrospect, this patient demonstrated signs and symptoms of potential malignancy on initial investigation (weight loss, anaemia and subcutaneous masses, which were subsequently proven to be metastases). No occult malignancies were detected. The number of incidental findings apparently warranting further investigation was five (23.8%), all of which were found to be benign.

The initial 2014-2015 search returned 256 cases, 51 of which were included (Fig. I). In 25/51 cases (49%), a CT of the chest was performed as well as a CT abdomen. Only potential malignancies in the abdomen were taken into account in this analysis: five malignancies were detected (9.8%), all, all of which retrospectively showed signs of potential malignancy on initial investigation (Table I). Two patients had a potential malignancy, one of which had symptoms/signs of malignancy on initial investigation (weight loss, anaemia) but did not have the suggested follow-up investigations at the time of this study, nine months later (patient A); one of which was anaemic but turned out to have a benign condition (patient B). Overall pick-up rate of early, occult malignancy in this group with no signs or symptoms of cancer on initial investigation was therefore zero. The age of the patients in whom malignancy was confirmed ranged from 53 to 78, median 68.

The number of incidental findings apparently warranting further investigation for the 2014-2015 data set was 10/51 (19.6%). On review, follow-up advice was deemed incorrect in four and correct in six (Table II).

Discussion

As expected, since publication of the 2012 NICE guidance, an increasing number of patients are being referred for an abdomino-pelvic CT, following presentation with an unprovoked VTE. The proportion of confirmed cancers in the 2014-2015 data set was 9.8%. This is comparable to recent studies, such as Carrier et al. which reported prevalence of 6.1% (95% CI 5.0-7.1) at presentation and 10.0% (95% CI 8.6-11.3) at 12 months.⁴ However, all of the malignancies (and potential malignancies) identified in our study had signs or symptoms of cancer on initial assessment, which would have triggered further investigation (Fig I). In half of the cases undergoing further imaging, a CT scan of the chest was incorrectly included in the request, leading to unjustified radiation exposure, extra cost and increased reporting times. Whilst we did not investigate the reasons for this, several explanations might be considered: the burgeoning number of guidelines and policies, time pressures in busy Acute Medical Units (AMU) and a lack of detailed clinical information on the CT requests, allowing radiologists to select the appropriate investigation.

Whilst the overall pick-up rate for malignancy in our study was around 10%, we did not pick-up any additional malignancies by following the NICE guidance. A recent, prospective Canadian multicentre randomised controlled trial, comparing screening for occult malignancy in unprovoked VTE without and with abdominal CT scans, described a lower overall incidence of occult malignancies than previously reported (3.8% vs. 10%) and, more

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Table II. Incidental findings reported on in the 2014-2015 data set

Age	Sex	Incidental CT finding	Radiological advice	Retrospective review	Further outcome
88	F	Abnormally enhancing and thickened cervix	Clinical assessment	Inappropriate: overall of normal findings	Referred to cervical rapid access clinic
88	F	Uterus attenuation change	USS	Appropriate	Abnormal endometrium. Gynaecology referral recommended. Died before referral appointment of unrelated cause.
80	F	Fibroid uterus ?adnexal mass	USS	Appropriate	NAD
81	F	Small ovarian cyst	USS	Inappropriate: below recommended referral size	Simple ovarian cyst
79	M	Non –specific lung nodules	CT follow up	Appropriate	Follow up CT not yet performed
60	M	Two tiny pulmonary nodules	Referral to lung MDT	Inappropriate; for CT follow up	Did not attend follow up
50	F	Pulmonary and adrenal nodule	MRI	Inappropriate–longstanding finding on review	Adenoma re-confirmed, biochemical monitoring and endocrine referral advised
64	M	Hilar node	CT follow up	Appropriate	Follow up CT not performed Lost to follow-up
68	F	Anterior mediastinal mass	No advice	Appropriate	Benign thymic mass
68	M	Lytic bone lesions	Bone scan	Appropriate	NAD

NAD – no abnormality detected

USS – ultrasound scan

MDT – multi-disciplinary team (meeting)

importantly in the context of our study, found no significant difference in detection rates between the two screening groups: 0.93% (95% CI 0.36 to 2.36) without CT vs. 1.18% (CI 0.51 – 2.74) with CT.⁵ The authors concluded that routine screening with CT of the abdomen and pelvis did not provide a clinically significant benefit.

Contrary to the zero pick-up rate of malignancy in the ‘NICE arm’ of the algorithm, incidental findings were detected in our cohort in approximately 20% of cases, many of which led to further investigation. Whilst many of these had no clinically relevant abnormality detected on further investigation, others did not receive the recommended follow-up. This has been described previously, for example, in a study by Kelly ME et al., which showed that 700 out of 1155 CT scans (61%) performed in the Emergency Department revealed incidental findings – 259 (22%) of which had additional investigations recommended by the reporting radiologist.⁶

In addition, some follow-up advice was deemed incorrect on subspecialist radiology review (Table 2). The inappropriate follow-up recommendations are partly explained by sub-specialty radiologists in our

Trust reporting these rapidly increasing numbers of “general” abdominal scans with inevitable limitations in knowledge of precise follow-up guidance on areas outside their expertise. This, for example, accounts for the high number of perceived incidental gynaecological findings in women over 80, leading to referral or further investigations, none of which turned out to be relevant. One case was incorrectly referred to an MDT for specialist assessment of the incidental finding; a common and unwarranted burden on such meetings. One case led to extensive further investigation of a benign adrenal nodule, which in retrospect had been present on previous imaging studies. Unnecessary patient anxiety, cost and potential harm caused by further investigation of incidental findings should be considered, both when requesting the scan and when interpreting the findings and recommending follow-up. The Canadian study mentioned above did not report on numbers and outcomes of incidental findings, but a prospective cohort study from 2011 by Van Doormaal FF et al., comparing limited and extensive cancer screening, reported a suspicion of cancer being raised in 30% of the patients screened with additional CT

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abdomen, with confirmation in only 2%.⁷ To put the radiation exposure of CT scans into perspective, as pointed out by Davies et al., the radiation dose of a CT scan is approximately that of 400 chest X-rays (or 3.3 years of background radiation) and radiation-induced cancer risk becomes a relevant consideration if the number needed to screen is very high.⁸

Whilst our findings are from a single tertiary teaching hospital Trust, it is likely that comparable challenges to guideline interpretation and implementation will be found in many other settings. It is clearly important for clinicians to recognise that the phrase “abdomino-pelvic CT should be considered” does not necessarily imply that this test “should always be performed”. Our data suggest that clinicians are justified in using their judgement to determine which patients require this investigation. The British Committee for Standards in Haematology also reflect this position in their recent guidance on aspects of cancer-related venous thrombosis and the outcomes of the recent Canadian study support this position.^{9, 5} A recent, large systematic review by Robertson L et al. published in the Cochrane database also concluded that the evidence for cancer screening effectiveness in unprovoked VTE is currently insufficient.¹⁰ It is also important to note that the NICE guidance does not recommend CT chest imaging in this situation. A robust system is required in the referring department to review all reports and clinically evaluate the relevance of

incidental findings and their recommendations; this will hopefully reduce the risk of unnecessary further investigation and loss to follow-up.

Whilst radiology services are currently under great pressure due to exponential increases in demand, our findings illustrate the risks and costs associated with increasing reporting pressures. Time to review previous imaging and obtain subspecialty consultation for incidental findings is increasingly sacrificed, but is essential to avoid unnecessary additional investigations and patient anxiety. Development of departmental guidance on the reporting of incidental findings, based on (locally modified) available guidance in the literature, will limit errors of interpretation and provide greater consistency and accuracy in follow up advice.¹¹

Although our conclusions are limited by the fact that this was a small, single centre, retrospective study, it is, to our knowledge, the first to assess the implementation of NICE Clinical Guideline 144 in a large UK hospital. Our data adds to the growing evidence-base that the value of CT scanning for detection of occult malignancy in VTE may be limited. It shows the challenges of correct implementation of new guidance and highlights the increasing problem of incidental findings on imaging studies.

Conflict of interest

The authors declare no conflicts of interest.

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