The route to diagnosis: emergency presentation of lung cancer

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Practice points

- Emergency presentation (EP) of cancer can be defined as the diagnosis of a new cancer as part of attending an emergency service such as Accident and Emergency, the Emergency Department or an Acute Medical Unit.
- EP is common in lung cancer, affecting up to 40% of new diagnoses, and is a feature of healthcare in all countries.
- EP of lung cancer is associated with specific patient demographics, such as older age and more co-morbidities, and certain disease characteristics including more advanced stage of disease.
- Patients diagnosed via the emergency route are less likely to receive anticancer therapy, and have a worse prognosis – especially 1 year survival – than those diagnosed through elective routes.
- The emergency route to diagnosis may be unavoidable, and indeed the best option, for some patients. In that situation, prompt input from specialist lung cancer medical and nursing teams is essential.
- The causes of EP of lung cancer are complex, and finding solutions is challenging.
- Reducing EP of lung cancer may be achieved through development of streamlined diagnostic pathways, public health campaigns, provision of decision-support tools for general practitioners, better communication between primary and secondary care, and improved access to diagnostic oncology services.
- Screening for lung cancer may have a positive effect on EP of lung cancer in the future.

A significant proportion of lung cancer patients are first diagnosed as part of an emergency presentation (EP) to acute medical services. This route to diagnosis is a strong negative predictor of survival, and is associated with age, deprivation and medical co-morbidities. Patients are less likely to receive anticancer treatment than those diagnosed through elective routes. The causes of EP of cancer are complex. When it is unavoidable, prompt input from specialist lung cancer services is needed. Preventing EP of lung cancer involves streamlined diagnostic pathways, public health campaigns about symptoms, decision-support tools for general practitioners, improved communication and access for primary and secondary care, and focus on vague symptoms. Reducing EP of lung cancer is important when improving outcomes and patient experience.

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Lung cancer is the commonest malignancy worldwide with over 1.8 million cases diagnosed in 2012, and is the commonest cause of cancer death with an annual mortality of almost 1.6 million [1]. The poor survival of lung cancer patients reflects the aggressive nature of the disease and late appearance of symptoms, but patient delay in presenting with symptoms is also important [2].

The UK has one of the lowest lung cancer survival rates in Europe [3]. Analysis of the excess deaths in England demonstrates that these predominantly occur within the first year of diagnosis [4], suggesting that the lower lung cancer survival is, at least in part, due to a higher number of deaths shortly after diagnosis. A significant proportion of lung cancer patients in England are first diagnosed with their disease as part of an emergency presentation (EP) to acute medical services and this route to diagnosis is a strong negative predictor of survival [5].

Understanding and preventing EP of lung cancer is central to improving the outcome for patients with lung cancer.

Definition of EP & limitations of data

There is no standard description of an EP of cancer, although is perhaps best defined as the diagnosis of a new cancer as part of attending an emergency service such as Accident and Emergency, the Emergency Department (ED) or an Acute Medical Unit.

The medical literature uses a variety of definitions including emergency or unplanned admission following attendance at Accident and Emergency, those not seen by a general practitioner (GP) prior to admission and patients who self-refer to an emergency service [6]. Nationally or regionally collected data often use proxy measures such as an emergency admission close to diagnosis, or admission on the day of referral [7].

The variations in definition of EP reflect the wider limitation of the available data: small patient numbers, single institution or single area studies, retrospective study design, lack of individual patient data and paucity of studies from outside the UK. Results are, therefore, subject to confounding factors and biases, which need to be taken into consideration when drawing conclusions.

Incidence of EP

Earlier studies struggled to establish an accurate rate of EP of lung cancer, with proportions ranging from 5 to 77% [8]. This reflects the challenges of identifying all patient diagnosed with lung cancer through each route, and differences in the definition of EP. A clearer understanding of routes to diagnosis and the true incidence of the EP of cancer came from the UK National Clinical Intelligence Network report in 2012. This landmark publication found that 40% of lung cancer patients present via the emergency route, one of highest proportions for any tumor type [5].

Although much of the data regarding EP of lung cancer have originated from the UK, it is an international problem that has been demonstrated in other countries such as New Zealand and the USA [7,9]. Proportions in Europe range from 13% (The Netherlands) to 35% (Portugal) [10].

Encouragingly, in England there has been a reduction in the frequency of EP of lung cancer over the past decade, from 39% in 2006 to 34% in 2013 [11,12]. This comparatively quick change is more likely to reflect the impact of changes in healthcare services, as opposed to changes in disease-related factors [13].

Impact of EP on lung cancer survival

Lung cancer patients who present via the emergency route have a lower survival compared with those diagnosed electively [5,14]. This difference persists at all stages up to 36 months after diagnosis, but is especially striking at earlier time points such as 1 month (95.2 vs 61.1% relative survival for those diagnosed via EP vs electively) and 3 months (79.5 vs 35.8%) [5,15]. Indeed, the risk of dying in the first month post-diagnosis is four-times higher for EP compared with non-EP patients [10]. The higher mortality with EP of lung cancer persists even when taking into account key confounding factors such as age, stage, and histological subtype [14,16].

Patient demographics

There is an association between increasing age and the EP of lung cancer [5,14,16–19]. Indeed, EP rises with age; 17% in the 66–69 age group, 25% in those aged 85 years and over [7]. In addition, lung cancer patients presenting via EP have lower socioeconomic status, greater social deprivation, display worse overall health and have a lower performance status [7,12,14,16,17,19,20]. Perhaps unsurprisingly, they are more likely to have medical co-morbidities and co-morbidity itself is a predictor of EP [7,14,16].

EP of lung cancer is associated with a higher prevalence in certain ethnic groups: people of Pacific origin in New Zealand, in the African-American population in the USA and, in the whole EP population not limited to lung cancer, patients of Asian ethnicity in England [7,9,17].

The association between gender and EP of lung cancer is less clear. Although female gender is listed as being associated with EP in some studies [14,21,22], others report no association with either sex [7].

Symptoms

Although those presenting as an emergency with lung cancer often describe a shorter duration of symptoms than their counterparts diagnosed through an elective route [23,24], in the majority of EP cases the symptoms were still present for more than 1 week [9,25]. For example, trigger symptoms (defined as the symptoms that the patient reported as being the reason for their emergency attendance to secondary care) are present for 2–12 weeks in 33% of patients, and for more than 12 weeks in 45% of patients prior to EP [26].

Distinguishing between patients presenting with lung cancer and those with symptoms related to lung other respiratory conditions is challenging. The majority of EP lung cancer patients have respiratory symptoms including chest pain, shoulder pain and dyspnea [26], with a range and nature similar to those diagnosed through other routes [27]. Therefore, the diagnostic difficulties are relevant to EP patients, and tools to aid clinical decision-making have the potential to allow more appropriate investigations.

Cancer characteristics

EP of lung cancer is associated with a higher stage of disease when compared with other routes to diagnosis [13]. For example, 30% of patients presenting via the emergency route have advanced (stage IV) disease, compared with 17% of patients presenting via outpatient urgent referral [11]. Stage is the single most important factor when determining prognosis, and lung cancer is particularly associated with advanced-stage disease at presentation.

Certain subtypes of thoracic malignancies, including small-cell lung cancer and mesothelioma, are over-represented in lung cancer patients presenting via the emergency route [10].

Impact of EP on patients & their management

Following EP, the diagnostic pathway is accessed rapidly. Yet patients are less likely to receive specialist lung oncology care compared with their counterparts diagnosed via the elective route [21] and delays in secondary care still occur at this point [9].

EP patients are less likely to have active treatment for their lung cancer, and less likely to undergo surgery or other treatments with curative intent [10]. This remains the case even when confounding factors such as age, socioeconomic status and tumor stage are taken into account [18]. Reflecting this picture, the diagnosis of lung cancer via the emergency route is more likely to be made on the basis of radiological findings [10,21].

The emergency route to diagnosis is associated with poorer patient experience, including that of subsequent cancer care, and is a significant additional burden on acute medical services [28,29].

Healthcare engagement prior to EP

For the majority of lung cancer patients presenting via EP, there are opportunities for earlier diagnosis because most have a relatively long history of symptoms, and 20–30% have been directly referral from primary care to acute medical services [26,30].

In response to their trigger symptoms, 54% of patient had consulted their GP prior to the EP, one quarter of whom had done so on three or more occasions. Of those who has been seen in primary care, a third were sent to the ED by the GP, while the remainder either attended ED of their own accord or were in the process of being investigated by either their GP or secondary care at the time of EP [26,31].

Opportunities for earlier diagnosis and prevention of EP extend to secondary care as well. Patients diagnosed via this route have more ED visits, more outpatient attendances and more hospital admissions in the preceding year [7]. This may reflect the greater co-morbidities of this patient group, greater use of emergency medical services, barriers to accessing primary care services, or may be evidence of missed opportunities to diagnose the cancer earlier [13]. Patients with better access to primary care, and for these services to be rated as providing a higher quality, are less likely to present via the emergency route [17,18]. Disparity in access to healthcare is therefore an important factor that may underlie EP for a significant proportion of lung cancer patients.

Although prior engagement with both primary and secondary care is a feature for many patients with EP of lung cancer, up to half directly attend ED in response to their trigger symptom. Consequently, there is a group of patients for whom EP may be the only realistic, and indeed best, route to diagnosis [20,26].

Prevention & management of EP

There is not one single solution to the problem of EP of lung cancer, however, there are a number of approaches by which diagnosis and survival can be improved for this vulnerable patient group. The majority of evidence relating to EP of lung cancer originates from the UK, and the remainder comes from a limited number of countries with developed healthcare services. Therefore, it is important to extend our understanding of the EP of lung cancer to include all countries and healthcare systems [13].

Patients who present the emergency route have potentially missed an opportunity to be diagnosed earlier in a more managed pathway. In many cases, EP can, therefore, be seen as an indicator of late diagnosis which itself can be caused by delays in presentation, primary care, between primary and secondary care, and in secondary care.

A number of innovative approaches have been tested in order to streamline diagnostic pathways for lung cancer. These include straight-to-computed tomography (CT) for those with abnormal chest x-rays (CXR), GP access to CT for those with concerning symptoms but normal CXR, radiology decision-support tools and improved communication pathways between radiologists and physicians [32]. In addition, independent reports and national cancer strategies have prioritized tackling the EP of cancer [33,34]. A best-practice, National Optimal Lung Cancer Pathway has been developed to shorten overall time to diagnosis, stipulating protocol-led triaging of referrals, rapid turnaround times for all investigations, hot reporting of all CXRs and subsequent CT scans, and daily rapid-access respiratory medicine cancer clinics. Maximum waiting times to diagnosis and treatment are set at 14 and 28 days, respectively [35]. Achieving this is a challenge for all healthcare systems, and will require service redesign.

There are a proportion of patients in whom EP is probably unavoidable, or indeed is the optimal route to diagnosis [20,26]. For these, the focus should be on support throughout the whole diagnostic journey. A clinical nurse specialist should be promptly available to all patients undergoing investigations for suspected lung cancer to act as their key worker [33]. Acute oncology, which focuses on patients with complications relating to their cancer diagnosis and treatment, or those with an EP of a new cancer, has an important role to play. Although the diagnostic pathway following EP is often swift, it should still be expedited to minimize delays. Patient should be registered on a timed multidisciplinary pathway so that diagnosis is as efficient, and the patient is afforded the same treatment opportunities, as those presenting via elective routes [33].

Given the complex events that contribute to an EP of lung cancer, decreasing the proportion of patients who present in this manner is challenging [36]. Campaigns to raise public awareness of the signs and symptoms of lung cancer can help promote earlier presentation to primary care and reduce the proportion of patients diagnosed via the emergency route [37]. EP lung cancer patients often show fear of cancer or fatalism, as well as emotional barriers to accessing medical services [38]. Public health messages need not only to be directed toward the patient demographic most at risk of EP but also need to address these barriers.

Low-dose CT screening can reduce lung cancer mortality [39] and has the potential to reduce the number of late lung cancer diagnoses, but has yet to undergo nationwide rollout in most countries. Screening for colorectal cancer has reduced EP rates and, therefore, CT screening for lung cancer has similar potential [13]. Any benefits with respect to reducing EP need to be balanced with the risks of overinvestigation and overdiagnosis.

Approximately one quarter of patients presenting via the emergency route describe a history of 'red flag' symptoms, which should prompt an urgent outpatient referral for suspected cancer [40], suggesting that earlier opportunities for elective investigation of patients are being missed. Lung cancer risk assessment and clinical decision-support tools can assist the GP. For example, the Cancer Decision Support Tool calculates a patient's risk for a specific type of cancer using prompts, symptom checkers and risk stratification lists based on symptoms, medical records and demographic data. Tested in 439 primary care practices, in 31% of cases it calculated a higher cancer risk than that perceived by the GP, and in 15% a lower risk. The tool influenced decisions in 33% of lung cancer consultations [41].

Improving communication and access between primary and secondary care is critical. Direct telephone or email access between GPs and secondary care consultants would speed discussion about high-risk cases. Other innovative schemes have pioneered open-access patient self-referral for chest radiographs, and the impact on subsequent routes to diagnosis is being assessed [42].

The ED is often used as a safe and quick access point to secondary care, even for those patients who do not require emergency medical care. Developing new outpatient pathways can prevent EP by providing GPs with access to rapid-access clinics for patients with clinical suspicion of cancer but who are too unwell to wait for an urgent outpatient appointment, or those in whom the likely tumor type is not clear [42]. The Danish pathway for patients with serious but nonspecific symptoms and signs of cancer is one of the pioneers in this area, and the importance of 'vague symptoms' is now being recognized in national health strategies [34,43].

Conclusion

The emergency presentation of lung cancer is a common route to diagnosis, and certain patient groups are especially at risk. The association with worse prognosis and poor patient experience makes it an important issue for all lung cancer services to address. Although the majority of data relating to the EP lung cancer come from the UK, it is truly an international problem. Although there is no single solution to EP lung cancer, enhancing elective diagnostic pathways and improving communication between healthcare professions are important first steps.

Future perspective

Further work addressing the limitations of the current data is required, so that the EP of lung cancer can be better appreciated and tackled in all countries. It is likely that greater recognition and understanding of EP of cancer that follows such work will inform public health strategies, allowing targeting of specific patient groups and diagnostic challenges, according to each country's priorities.

Looking forward, pilot projects will demonstrate the feasibility and acceptability of innovative diagnostic strategies, such as primary care access to CT scanning [32], with the most promising taken forward for rollout into routine clinical services.

Improving the entire lung cancer diagnostic pathway, aiming for a more streamlined process has the potential to reduce the rate of EP of lung cancer. National approaches, such as the National Optimal Lung Cancer Pathway will be piloted, with the cost and resource implications better understood.

Low-dose CT screening for lung cancer is likely to be implemented in a number of countries in the coming years. As with screening for other malignancies, this is likely to reduce the incidence of EP, but it will come at a financial cost and a cost of overinvestigation and overdiagnosis.

In summary, within the next decade the EP of lung cancer will be internationally recognized as the problem it represents, but rates will be falling as this range of measures is introduced to improve the route to diagnosis of patients with thoracic malignancies.

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References

- 1 Ferlay J, Soerjomataram I, Dikshit R *et al.* Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int. J. Cancer* 136(5), E359–E386 (2015).
- 2 Hamilton W, Peters TJ, Round A, Sharp D. What are the clinical features of lung cancer before the diagnosis is made? A population based case-control study. *Thorax* 60(12), 1059–1065 (2005).
- 3 De Angelis R, Sant M, Coleman MP *et al.* Cancer survival in Europe 1999–2007 by country and age: results of EURO CARE-5—a population-based study. *Lancet Oncol.* 15(1), 23–34 (2014).
- 4 Holmberg L, Sandin F, Bray F *et al.* National comparisons of lung cancer survival in England, Norway and Sweden 2001–2004: differences occur early in follow-up. *Thorax* 65(5), 436–441 (2010).
- 5 Elliss-Brookes L, McPhail S, Ives A *et al.* Routes to diagnosis for cancer - determining the patient journey using multiple routine data sets. *Br. J. Cancer* 107(8), 1220–1226 (2012).
- 6 Jiwa M, Maujean E, Spilsbury K, Threlfall T. The trajectory of lung cancer patients in Western Australia –a data linkage study: still a grim tale. *Lung Cancer* 70(1), 22–27 (2010).
- 7 Sikka V, Ornato JP. Cancer diagnosis and outcomes in Michigan EDs vs other settings. *Am. J. Emerg. Med.* 30(2), 283–292 (2012).
- 8 Neal RD, Allgar VL, Ali N *et al.* Stage, survival and delays in lung, colorectal, prostate and ovarian cancer: comparison between diagnostic routes. *Br. J. Gen. Pract.* 57(536), 212–219 (2007).
- 9 Beatty S, Stevens W, Stevens G, Kolbe J, Cox B. Lung cancer patients in New Zealand initially present to secondary care through the emergency department rather than by referral to a respiratory specialist. *N. Z. Med. J.* 122(1294), 33–41 (2009).
- 10 Newsom-Davis T, Berardi R, Cassidy N *et al.* Emergency diagnosis of lung cancer: an international problem [abstract]. *J. Clin. Oncol.* 33, 6536 (2015).
- 11 National Cancer Intelligence Network. Routes to diagnosis by stage, 2012–2013 (2016). www.ncin.org.uk/publications/routes_to_diagnosis
- 12 Abel GA, Shelton J, Johnson S, Elliss-Brookes L, Lyratzopoulos G. Cancer-specific variation in emergency presentation by sex, age and deprivation across 27 common and rarer cancers. *Br. J. Cancer* 112(Suppl. 1), S129–S136 (2015).
- 13 Zhou Y, Abel GA, Hamilton W *et al.* Diagnosis of cancer as an emergency: a critical review of current evidence. *Nat. Rev. Clin. Oncol.* 14(1), 45–56 (2017).
- 14 Beckett P, Tata LJ, Hubbard RB. Risk factors and survival outcome for non-elective referral in non-small cell lung cancer patients – analysis based on the National Lung Cancer Audit. *Lung Cancer* 83(3), 396–400 (2014).
- 15 Public Health England. Routes to diagnosis 2015 update: lung cancer (2015). www.ncin.org.uk/publications/routes_to_diagnosis

- 16 Mcphail S, Elliss-Brookes L, Shelton J *et al*. Emergency presentation of cancer and short-term mortality. *Br. J. Cancer* 109(8), 2027–2034 (2013).
- 17 Bottle A, Tsang C, Parsons C, Majeed A, Soljak M, Aylin P. Association between patient and general practice characteristics and unplanned first-time admissions for cancer: observational study. *Br. J. Cancer* 107(8), 1213–1219 (2012).
- 18 Tataru D, Jack RH, Lind MJ, Moller H, Luchtenborg M. The effect of emergency presentation on surgery and survival in lung cancer patients in England, 2006–2008. *Cancer Epidemiol.* 39(4), 612–616 (2015).
- 19 Tsang C, Bottle A, Majeed A, Aylin P. Cancer diagnosed by emergency admission in England: an observational study using the general practice research database. *BMC Health Serv. Res.* 13, 308 (2013).
- 20 Mitchell ED, Pickwell-Smith B, Macleod U. Risk factors for emergency presentation with lung and colorectal cancers: a systematic review. *BMJ Open* 5(4), e006965 (2015).
- 21 Melling PP, Hatfield AC, Muers MF *et al*. Lung cancer referral patterns in the former Yorkshire region of the UK. *Br. J. Cancer* 86(1), 36–42 (2002).
- 22 Raine R, Wong W, Scholes S, Ashton C, Obichere A, Ambler G. Social variations in access to hospital care for patients with colorectal, breast, and lung cancer between 1999 and 2006: retrospective analysis of hospital episode statistics. *BMJ* 340, b5479 (2010).
- 23 Barrett J, Hamilton W. Pathways to the diagnosis of lung cancer in the UK: a cohort study. *BMC Fam. Pract.* 9, 31 (2008).
- 24 Porta M, Fernandez E, Belloc J, Malats N, Gallen M, Alonso J. Emergency admission for cancer: a matter of survival? *Br. J. Cancer* 77(3), 477–484 (1998).
- 25 Hargarten SW, Richards MJ, Anderson AJ. Cancer presentation in the emergency department: a failure of primary care. *Am. J. Emerg. Med.* 10(4), 290–293 (1992).
- 26 Forbes L, Sarafraz-Shekary N, Kaushal A, Ramirez A-J, Hughes C, Newsom-Davis T. What explains diagnosis of lung or bowel cancer as an emergency? Presented at: *10th NCRI Annual Conference*. Liverpool, UK, 2–5 November 2014.
- 27 Royal College of General Practitioners. National audit of cancer diagnosis in primary care (2011). www.rcgp.org.uk/policy/rcgp-policy-areas/national-audit-of-cancer-diagnosis-in-primary-care.aspx
- 28 NHS England. High quality care for all, now and for future generations: transforming urgent and emergency care services in England—Urgent and Emergency Care Review End of Phase I Report (2013). www.england.nhs.uk/wp-content/uploads/2013/06/urg-emerg-care-ev-bse.pdf
- 29 Quality Health. Cancer Patient Experience Survey 2014 National Report (2014). www.quality-health.co.uk/surveys/national-cancer-patient-experience-survey
- 30 National Cancer Intelligence Network. Routes to diagnosis: exploring emergency presentations (2013). www.ncin.org.uk/publications/routes.to.diagnosis
- 31 Hamilton W. Diagnosing symptomatic cancer in the NHS. *BMJ* 351, h5311 (2015).
- 32 Cluster ALCP. Final Report. Accelerate, Coordinate, Evaluate (ACE) Programme: an early diagnosis of cancer initiative supported by NHS England, Cancer Research UK and Macmillan Cancer Support (2017). www.cancerresearchuk.org/health-professional/diagnosis/ace-programme
- 33 British Lung Foundation. Tackling emergency presentation of lung cancer: an expert working group report and recommendations (2015). www.blf.org.uk/sites/default/files/BLF_lung_cancer_report_2015.pdf
- 34 Independent Cancer Taskforce. Achieving world-class cancer outcomes: a strategy for England 2015–2020 (2015). www.cancerresearchuk.org/sites/default/files/achieving-world-class-cancer-outcomes.-a-strategy-for-england_2015-2020.pdf
- 35 Lung Cancer Clinical Expert Group. National Optimal Lung Cancer Pathway for suspected and confirmed lung cancer: referral to treatment (2016). www.cancerresearchuk.org/sites/default/files/optimal_lung_cancer_pathway.pdf
- 36 Lyratzopoulos G, Saunders CL, Abel GA. Are emergency diagnoses of cancer avoidable? A proposed taxonomy to motivate study design and support service improvement. *Future Oncol.* 10(8), 1329–1333 (2014).
- 37 Ironmonger L, Ohuma E, Ormiston-Smith N, Gildea C, Thomson CS, Peake MD. An evaluation of the impact of large-scale interventions to raise public awareness of a lung cancer symptom. *Br. J. Cancer* 112(1), 207–216 (2015).
- 38 Birt L, Hall N, Emery J *et al*. Responding to symptoms suggestive of lung cancer: a qualitative interview study. *BMJ Open Respir. Res.* 1(1), e000067 (2014).
- 39 The National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N. Engl. J. Med.* 365(5), 395–409 (2011).
- 40 Thames Valley Strategic Cancer Network. Saving 5,000 lives project – cancer networks supporting primary care (2013). <http://tvscn.nhs.uk/wp-content/uploads/2014/05/Cancer-Strategic-Clinical-Network-Proposal-for-Cancer-Clinical-Network-Groups-February-2014V3.pdf>
- 41 Moffat J, Ironmonger L, Green T. Clinical Decision Support Tool for Cancer (CDS) Project: evaluation report to the Department of Health (2014). www.cancerresearchuk.org/sites/default/files/cds_final_310714.pdf

- 42 Cancer Research UK. Cancer Research UK: ACE Programme (2016). www.cancerresearchuk.org/health-professional/diagnosis/ace-programme
- 43 Ingeman ML, Christensen MB, Bro F, Knudsen ST, Vedsted P. The Danish cancer pathway for patients with serious non-specific symptoms and signs of cancer-a cross-sectional study of patient characteristics and cancer probability. *BMC Cancer* 15, 421 (2015).