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RESEARCH ARTICLE

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Validation of the Swedish National Inpatient Register for the diagnosis of pulmonary embolism in 2005

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Abstract

The Swedish National Inpatient Register (NPR) has near-complete coverage of in-hospital admissions and ICD codes in Sweden. Acute pulmonary embolism (PE) is a serious condition presenting challenges regarding diagnosis, treatment, and follow-up. Here we aimed to validate the accuracy of acute PE diagnosis in the NPR, investigational findings, antithrombotic treatment, and follow-up of PE patients in Sweden. From a nation-wide cohort of all patients with in-hospital diagnoses of acute PE (ICD-10-SE codes I26.0–I26.9) in 2005 ($n = 5793$), we selected those from two Swedish regions for thorough manual review of hospital records. We identified 599 patients with PE diagnoses according to the ICD-10 coding system. We excluded 58 patients with admissions related to previous PE (47; 8%) or incorrect ICD codes (11; 2%), leaving 501 patients with probable PE diagnoses. We confirmed the diagnosis in 441 (79%) cases, which was based on imaging (435 patients; 73%) or autopsy (6; 1%). In the remaining 60 (11%) cases, the PE diagnosis was based on clinical findings and can therefore not be confirmed. Of the surviving patients with PE, 231 (47%) were offered follow-up within 6 months after the acute event. At follow-up, 67 patients (29%) had symptoms requiring clinical attention (dyspnoea or reduced general condition). The Swedish NPR showed acceptable accuracy for PE diagnosis, and could be reliably used for register-based research regarding acute PE.

KEYWORDS
clinical presentation, epidemiology, follow-up, pulmonary embolism, register

Abbreviations: CT, computer tomography; CTEPH, chronic thromboembolic pulmonary hypertension; ICD-10, International Classification of Diseases, version 10; IQR, interquartile range; LMHW, low molecular weight heparin; NPR, National Patient Register; NOAC, novel oral anticoagulants; PE, pulmonary embolism; OAC, oral anticoagulants; V/Q, ventilation/perfusion.

INTRODUCTION

The Swedish National Inpatient Register (NPR), hosted by the Swedish National Board of Health and Welfare, was established in 1964 and records information about all in-patient care in Sweden. Since 1987, the national coverage is over 99%, since reporting is mandatory for all healthcare providers. The collected information includes where and when the in-patient care occurred, with associated diagnoses and procedures coded according to the International Classification of Disease (ICD). Since 1997, the Swedish version ICD-10-SE has been used, and the NPR validity is reported to be high.[1]

The Swedish NPR is a valuable resource for large-scale register-based studies since it enables the cost-effective collection and analysis of large quantities of data. Furthermore, the unique Swedish identity number enables cross-linking between the NPR and other data sources, such as hospital records. One notable limitation is that many conditions are more complex than reflected by the ICD codes. Thus, it is essential to perform repeated validation studies with comparison to clinical data, which can also help in detecting eventual drifts over time in coding.

Acute pulmonary embolism (PE) is a serious condition with many nonspecific symptoms, which can imitate many other pulmonary and cardiac conditions.[2,3] The methods for acute PE detection have improved over recent decades, with the introduction of better and more accessible computed tomography (CT) angiography and echocardiography, and the widespread use of D-dimer testing together with clinical risk assessment scores, such as the Well's score.[2]

Despite these improvements, challenges persist in terms of acute PE diagnosis, treatment, and follow-up.

One recent study demonstrated that PE diagnosis according to the Swedish NPR has a positive predictive value of 81%.[4] However, that study included a restricted age span set based on participation in a local cohort, and only included cases of first-ever PE and where radiological examination was performed.

Our research group has identified a nation-wide cohort of all in-hospital care events with a diagnosis of PE in 2005, based on the Swedish NPR, and we identified significantly increased short- and long-term mortality in the PE cohort compared with in the normal population.[6]

In the present study, we aimed to validate the accuracy of PE diagnosis, investigational findings, treatment, and follow-up in this cohort.

METHODS

Subjects

We established a nation-wide cohort of all subjects with an in-hospital diagnosis of acute PE in 2005 (ICD-10-SE codes I26.0–I26.9), either as a main or subsidiary diagnosis, irrespective of number and positions of other ICD codes. Altogether, this cohort included 5793 unique individuals. If a patient had several admissions in 2005, only the first was included.[6]

From this cohort, we identified all subjects who received in-patient care at three hospitals located in Västerbotten County ($n = 195$), and at three hospitals located in Västra Götaland Region ($n = 364$), constituting approximately 10% of the national cohort. Both university and district hospitals were included, from regions of Northern and Southwest Sweden that included both densely populated and sparsely populated areas. Two of the authors (AI and HK) conducted a thorough manual review of all corresponding hospital records, using a standardized form to collect information regarding risk factors, symptoms and clinical signs at admission, investigational findings, treatment(s) given, and follow-up procedures.

An event of acute PE was considered validated when the diagnosis was based on imaging (CT angiography or ventilation-perfusion [V/Q] scintigraphy) or autopsy. In cases of clinically diagnosed PE, we analysed the other ICD-10-SE codes to better understand why the treating physician chose not to perform imaging.

Statistical methods

Categorical variables are expressed as frequencies and proportions, and continuous variables are expressed as medians with interquartile range (IQR). All data were analysed using IBM SPSS statistics software version 25.

RESULTS

Altogether, 559 subjects were identified as having the ICD–10–SE code I26.0–I26.9 as a primary or subsidiary diagnosis from an in-hospital admission within the selected regions. PE diagnosis was confirmed by imaging in 435 patients (69% CT angiography, 6% V/Q scintigraphy, and 2% both CT angiography and V/Q scintigraphy) (Table 1), and by autopsy in 6 patients (1%). In 60 patients (11%), PE was clinically diagnosed without radiological confirmation, and therefore not considered to be

validated diagnoses of PE. In 11 patients (2%), the acute PE diagnosis was incorrect, and in 47 patients (8%), the PE diagnosis was correct but was related to a previous admission and was thus not considered an acute PE event and was regarded as incorrectly registered. These latter 58 patients were excluded from further analysis.

Among the 60 patients with clinical PE not confirmed by imaging, 15% ($n = 9$) had deep venous thrombosis; 10% ($n = 6$) had documented cognitive failure; 8% ($n = 5$) had significant renal failure; 22% ($n = 13$) had a known malignancy; and 27% ($n = 16$) had another indication for anticoagulant treatment, mainly atrial fibrillation ($n = 14$). In 45% ($n = 27$), PE was not the main diagnosis. Among the patients clinically diagnosed with PE, 10% ($n = 6$) received thrombolytic therapy.

TABLE 1 Validation of the acute PE diagnosis

	n (%)
Diagnosis confirmed by imaging[a]	435 (78)
CT angiography	387 (69)
V/Q scintigraphy	36 (6)
Both CT angiography and V/Q scintigraphy	12 (2)
Diagnosis confirmed by autopsy	6 (1)
Clinical diagnosis without imaging[b]	60 (11)
Previous PE diagnosis[c]	47 (8)
Incorrect diagnosis	11 (2)

Abbreviations: CT, computer tomography; PE, pulmonary embolism; V/Q scintigraphy, ventilation and perfusion scintigraphy.

[a]Diagnosis objectively confirmed with either CT angiography or V/Q scintigraphy.

[b]Clinical diagnosis of PE not verified with CT angiography or V/Q scintigraphy.

[c]Diagnosis of acute PE was incorrectly recorded and was actually related to a previous hospital admission.

Among the 441 patients with confirmed PE diagnosis (either by imaging or autopsy), 54% were women. The median (IQR) ages were 77 (17) years for women, and 69 (19) years for men (Table 2). A total of 251 echocardiograms were performed at the time of diagnosis, of which 83 included an estimation of the right ventricular systolic pressure. The estimated median (IQR) right ventricular systolic pressure was 50 (22) mmHg.

A total of 44 patients (10%) died: 0.5% at admission and 10% during the in-hospital stay. During the acute phase, 5% ($n = 22$) received thrombolysis. Subsequent initial treatment regimens included warfarin combined with low-molecular-weight heparin (LMHW) (61%), LMHW monotherapy (33%), and warfarin monotherapy (2%). Of those who received LMHW as monotherapy, 45% had a cancer diagnosis with active treatment during the last year.

Among the surviving patients with confirmed PE diagnosis, only 214 (49%) were offered a follow-up visit within 6 months after the acute PE event. At follow-up, 51 patients (24%) were still dyspnoeic or had a reduced general condition, and another eight patients (4%) reported new or worse dyspnoea or further reduced general condition compared to at the time of the acute PE event.

TABLE 2 Characteristics at admission, treatment, and follow-up

	Available data	Yes *n* (%)
Gender, Female/Male	441/441	237 (54)/204(46)
Age, Female/Male	441/441	77 (17)/69(19)
Echocardiography performed at admission	440/441	251 (57)
Median estimated right ventricular pressure on echocardiography	83/251	50 (22)
Thrombolysis	339/441	22 (5)
Warfarin—monotherapy	441/441	11 (2)
LMHW—monotherapy	441/441	147 (33)
Combination-therapy with Warfarin and LMHW	441/441	269 (61)
Follow-up visit within 6 months after PE	397/441	214 (49)
Remaining symptoms of dyspnea at follow-up	214/214	51 (24)
Increased symptoms of dyspnea at follow-up	214/214	8 (4)
No remaining symptoms of dyspnea at follow-up	214/214	155 (72)
Echocardiography performed at follow-up	214/214	44 (21)

Note: Values shown are numbers and percent, or median (IQR) for continuous variables.

Abbreviation: LMHW, low molecular weight heparin.

The majority ($n = 155$; 72%) considered themselves to be completely recovered.

DISCUSSION

In this cohort, 78% of the acute PE events were confirmed by imaging, mainly by CT–angiography, which corresponds with recent published data.[4] Additionally, 1% were confirmed by autopsy, and 11% were diagnosed based on clinical presentation, which may be correct but cannot be verified. Only 10% were incorrectly diagnosed as acute PE, demonstrated that the Swedish NPR has an acceptable accuracy for PE diagnoses, and could be reliably used for register-based research regarding acute PE.

Echocardiography is not mandatory in the diagnostic process of PE but can be performed for prognostic evaluation or as a part of the differential diagnostics. In this cohort, there were surprisingly few echocardiograms were performed during the acute phase, but we hypothesize that this frequency is higher today as echocardiography is now generally more accessible.

Oral anti-coagulation (OAC) with warfarin, or with novel oral anticoagulants (NOAC), is the recommended treatment for acute PE.[2] Despite this, we found a surprisingly high frequency of monotherapy with LMHW. Physicians may have refrained from using warfarin not only in patients with malignancies and severe renal failure but also in fragile patients and in situations where low adherence was suspected. This frequency may be lower at the present time due to increased use of NOAC.

We found a low proportion (49%) of follow-up visits. This is unsatisfactory considering that approximately half of those seen at follow-up exhibited remaining or new/worse symptoms that required clinical attention. Unfortunately, there is no reliable data describing the 6-month mortality rate in this specific cohort. Previous studies show a relatively high mortality rate during the first 6 months after an acute PE, which is likely to affect the number of possible follow-up visits.[5] Chronic thromboembolism pulmonary hypertension (CTEPH) is a feared condition after acute PE, but seems to be a relatively uncommon complication.[6,7] Lately, there has been greater focus on a condition termed post-PE-syndrome, which is associated with both dyspnoea and reduced physical capacity[8,9] and we have recently shown that patients with previous PE had substantially higher prevalences of both exertional dyspnea (53.0% vs. 17.3%) and wake-up dyspnea (12.0% vs. 1.7%) compared to control subjects.[10]

Importantly, follow-up also plays a major role in the investigation of possible underlying diseases, such as coagulopathies and malignancies.

To our knowledge, there are no previous analyses of follow-up routines after acute PE in Sweden. The recently updated ESC guidelines on acute PE strongly emphasize the need for appropriate follow-up. It is recommended to search for VTE recurrences, bleeding complications, malignancies, and persistent dyspnoea, which may indicate the development of CTEPH.[2] In our previous report, we demonstrated that both short- and long-term mortality rates were high after acute PE, irrespective of previous or concomitant malignant disease.[5] This highlights the need for establishment of adequate follow-up routines after an acute PE.

The strength of this study is the complete nation-wide sample of all in-hospital care for acute PE occurring during one year, including patients of all ages, and irrespective of comorbidities. Furthermore, we collected only pre-specified and standardized data from hospital records. Another strength of this study is its size. We validated approximately 10% of all cases of acute PE in Sweden in 2005.

Even if the diagnostic algorithm for PE has not changed in Sweden since 2005, an important limitation of the study is we do not have data from a more recent cohort of PE patients, and a contemporary follow-up is needed to establish if the present guidelines are followed.

In addition, only PE events diagnosed during in-patient care were included. Cases of acute PE that received out-patient treatment (probably very few) or treatment in nursing homes were not included. Furthermore, patients who died from an acute PE before hospital admission were not included. Additionally, the presented numbers and proportions are based on available data, which were extracted from hospital files with varying quality and completeness.

CONCLUSION

The Swedish NPR showed acceptable accuracy for PE diagnosis, and could be reliably used for register-based research regarding acute PE.

Our analysis revealed noteworthy aspects of treatment, diagnostic routines, and follow-up that require attention and improvements. But even though the diagnostic algorithm has not changed, the treatment regime of PE has changed significantly after the introduction of NOAC's. Furthermore, the knowledge regarding long-term consequences after PE has increased (the risk for CTEPH) which has (hopefully) lead to better follow-up after an acute PE.

Therefore, we are in need of future studies to evaluate these changes over time, and its impact on clinical outcomes.

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CONFLICT OF INTERESTS

S.S. is an advisory board member and received speaker's honoraria from Actelion, Bayer, and MSD, for presentations on topics outside the submitted study. T.A. received speaker's honoraria from Actelion.

ETHICS STATEMENT

This study was conducted in compliance with the Declaration of Helsinki, and was approved by the Regional Ethics Review Board in Umeå, Sweden (07-074). The Ethics Board at the Swedish National Board of Health and Welfare reviewed and approved the extraction of data from the Swedish NPR. Department heads granted access to local hospital records.

AUTHOR CONTRIBUTIONS

Stefan Söderberg had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Stefan Söderberg, Therese Andersson, Anja Isaksson, Hesham Khalil, Leif Lapidus, and Bo Carlberg, contributed substantially to the study design, data analysis, and interpretation. Therese Andersson drafted the manuscript and all authors critically revived the final manuscript.

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