

Pulmonary embolism in young people

Trends in Germany from 2005 to 2011

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Schlüsselwörter

Lungenembolie, DRG-Statistik, stationäre Patienten, Geschlechter

Zusammenfassung

Ziele: Es gibt eine anhaltende Diskussion über die Auswirkungen der hormonalen Kontrazeption auf die Inzidenz von venösen Thromboembolien (VTE) bei jungen Frauen. Spezifische Daten für die Größe des Problems und ihre Veränderungen in den letzten Jahren in Deutschland sind nicht verfügbar. Daher untersuchten wir die Häufigkeit von VTE bei hospitalisierten jungen Menschen und analysierten geschlechtsspezifische Unterschiede. **Patienten und Methoden:** Detaillierte Listen aller Lungenembolien (LE), kodiert als I26, und tiefer Venenthrombosen (TVT), kodiert als I80, bei Patienten im Alter von 10 bis 39 Jahre, die in den Jahren 2005 bis 2011 ins Krankenhaus eingeliefert worden waren, stellte das Statistische Bundesamt zur Verfügung. **Ergebnisse:** Beginnend im Alter von 12–13 Jahren wurde für Frauen im Vergleich zu Männern eine höhere Anzahl von LE und TVT als Hauptdiagnose dokumentiert. Dieser geschlechtsspezifische Unterschied verschwindet im Alter von 32–33 Jahren. Dieser Unterschied in der Gesamtzahl der LE als Hauptdiagnose zwischen Männern und Frauen innerhalb dieses Lebensabschnitts von 20

Jahre erhöhte sich von 318 in 2005 auf 606 im Jahr 2010 und sank auf 505 im Jahr 2011. Die Differenzierung in LE mit und ohne akutes cor pulmonale zeigte insbesondere eine spezifische Erhöhung der LE ohne akutes cor pulmonale bei jungen Frauen innerhalb dieser sieben Jahre. Ähnliche Änderungen konnten nicht für TVT als Hauptdiagnose gezeigt werden. **Schlussfolgerung:** Die präsentierten Daten aus der deutschen DRG-Statistik zeigen einen disproportional höheren Anstieg der Hospitalisierung junger Frauen mit Lungenembolie als Hauptdiagnose in den vergangenen Jahren. Die möglichen Ursachen der hormonalen Kontrazeption für diesen Anstieg müssen weiter aufgeklärt werden.

Keywords

Pulmonary embolism, hospitalised patients, DRG statistics, gender

Summary

Objectives: There is an ongoing discussion about the impact of hormonal contraception on the incidence of venous thromboembolism (VTE) in young women. Specific data of the significance of this problem and its changes in recent years in Germany are not available. Thus, we analyzed the incidence of VTE in hos-

pitalized young patients and looked for gender-specific differences. **Patients and methods:** Detailed lists of all pulmonary embolisms (PE) coded as I26 and deep vein thrombosis (DVT) coded as I80 in patients aged 10 to 39 years hospitalized in the years 2005 to 2011 were provided by the Federal Statistical Office. **Results:** Beginning at the age of 12–13 years girls have higher numbers of PE and DVT documented as principal diagnosis, as compared to boys. This gender-specific difference disappears at the ages of 32–33 years. The difference in total numbers of PE (as principal diagnosis) between women and men within this 20-year time span increased from 318 in 2005 to 606 in 2010 and decreased to 505 in 2011. Stratifying the cases of PE according to presence or absence of cor pulmonale, the analysis showed a specific increase of PE in young women without cor pulmonale within the period of seven years between 2005 and 2011. Similar changes could not be shown for DVT as principal diagnosis. **Conclusion:** The presented data from the German DRG statistics show a disproportionately higher increase of young women hospitalised for pulmonary embolism as principal diagnosis in recent years. The possible impact of hormonal contraception on this increase has to be further elucidated.

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Lungenembolie bei jungen Menschen Trends in Deutschland von 2005 bis 2011

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The overall incidence of venous thromboembolism (VTE) does not appear to vary significantly by sex, as evidenced by a lack of consistency in the magnitude and even the direction of effect of sex in a variety of epidemiological studies of varying design (5). The main influence of gender on VTE is the relationship between female gender and several well-recognized clinical risk factors for VTE:

- hormonal contraceptive use,
- hormone replacement therapy,
- estrogen receptor modulator therapy,
- pregnancy.

The majority of recent studies have demonstrated – as compared with non-users – a threefold increased risk of VTE in current users of medium- and low-dose combined oral contraceptives (COCs) with

- norethisterone,
- levonorgestrel or
- norgestimate.

The same studies have demonstrated a six-fold increased risk of VTE in users of combined pills with the so called third-generation or fourth-generation COCs (1, 3, 9)

- desogestrel,
- gestodene,
- drospirenone or
- cyproteroneacetate.

Especially the effect of COCs containing drospirenone has been studied. According to a case control study from the U.S. based on 186 newly diagnosed, idiopathic cases of VTE matched with 681 controls, the risk of non-fatal VTE among users of oral contraceptives containing drospirenone seems to be around twice as high as that of users of oral contraceptives containing levonorgestrel (2). Others could not support these findings (8). Thus, there is an ongoing discussion about the use of these oral contraceptives but concrete data from Germany are lacking.

In 2009, we published data based on the German DRG statistics showing the gender-specific differences in young people aged 10 to 39 years hospitalised for pulmonary embolism as principal diagnosis (6). The data showed that there is a sharp increase in hospitalization with PE in fe-

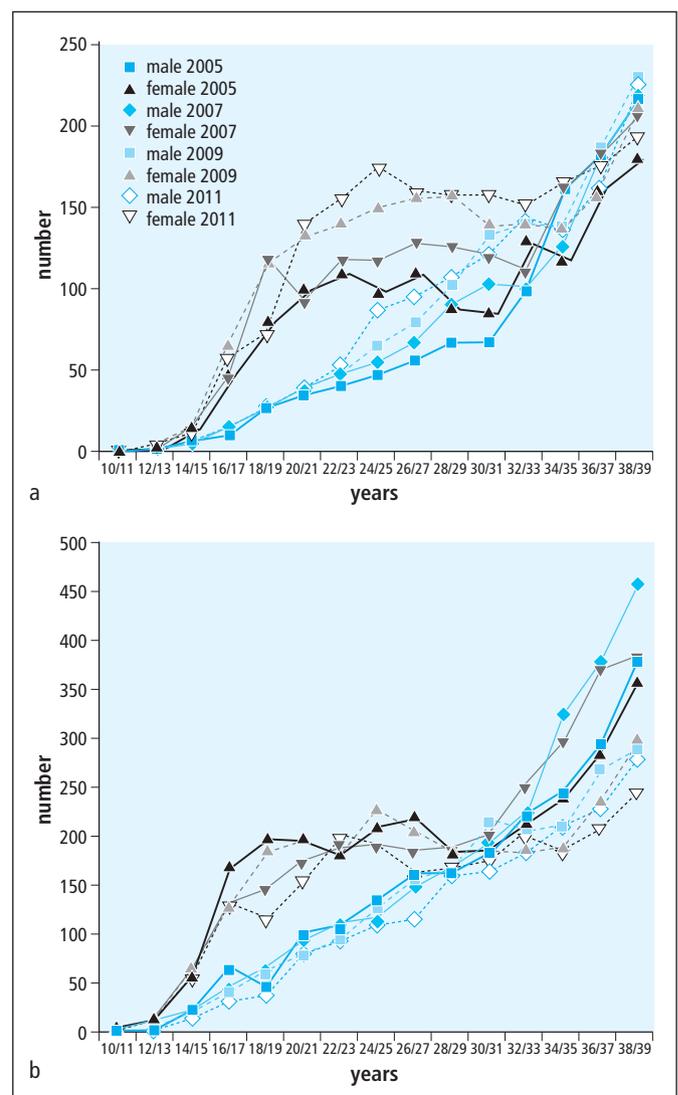
males beginning with 12–13 years, as compared to males. Up to the ages of 32 to 33 years women were hospitalized more often with PE than men. Even so, the absolute numbers are small for both sexes. We recommended this method to monitor overall trends of VTE in young women in Germany. It is because of the higher numbers of VTE that we looked for trends that possibly may reflect some influences of new hormonal contraceptives.

Patients and methods

The national statistics (DRG statistics) published by the Federal Statistical Office includes data from all hospitals in Germany that use the DRG system (2). These

hospitals are legally obliged to provide extensive data on hospital treatment, including demographic data, diagnoses, co-morbidities, complications, and procedures to the Institute for the Hospital Remuneration System (InEK), which uses the data for a yearly adaptation of the German DRG system and transmits them to the Federal Statistical Office.

From 2005 to 2011 all diagnoses were coded with the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), which was adapted for Germany by the German Institute for Medical Documentation and Information (DIMDI) as ICD-10 German Modification (ICD-10-GM) in the corresponding annual version.



Tab. 1 Number of all hospitalised male and female patients aged from 10 to 39 years with PE and DVT documented as principal diagnosis and the delta between both groups in the years 2005 to 2011 (percentages as the increase or decrease compared to the numbers of the year 2005)

principal diagnosis in the year	deep vein thrombosis			pulmonary embolism		
	males	females	delta	males	females	delta
2005	1533	2071	538	1023	1341	318
2006	1605 (+5%)	2050 (-1%)	445 (-17%)	1132 (+11%)	1511 (+13%)	379 (+19%)
2007	1478 (-4%)	2048 (-1%)	606 (+13%)	1086 (+6%)	1549 (+16%)	463 (+46%)
2008	2036 (+33%)	2613 (+26%)	577 (+7%)	1173 (+15%)	1659 (+24%)	486 (+53%)
2009	1689 (+110)	2504 (+121)	515 (-4%)	1195 (+17%)	1732 (+29%)	537 (+69%)
2010	1887 (+23%)	2336 (+13%)	449 (-17%)	1236 (+21%)	1842 (+37%)	606 (+91%)
2011	1758 (+8%)	2230 (+8%)	472 (-12%)	1232 (+20%)	1787 (+33%)	505 (+59%)

- PE was coded as
 - I26.0 (PE with acute pulmonary hypertension) and
 - I26.9 (PE without acute pulmonary hypertension).
- Deep vein thrombosis (DVT) was coded as I80, this code summarizing
 - deep vein thrombosis (I80.1-I80.3),
 - superficial vein thrombosis (I80.0) of the lower extremity and
 - DVT in general of unspecified localization (I80.8, I80.9).

(I26.0 and I26.9) as principal diagnosis and those with deep vein thrombosis (DVT) (I80.0; 80.1, 80.2, 80.3, 80.8, 80.9) as principal diagnosis. Calculations were done using Microsoft® Excel 2003 and Microsoft® Access 2003.

Results

Beginning at the age of 12–13 years, females had a higher incidence of PE and DVT documented as principal diagnosis than men (▶ Fig. 1). This gender-specific difference disappeared at the age of 32 to 33 years. This effect manifested constantly over the course of those seven years.

The total numbers of young males and females hospitalized with PE as principal

diagnosis increased from 2005 to 2010 but decreased in 2011 (▶ Tab. 1). The difference in total numbers of PE (as principal diagnosis) between women and men within this 20-year time span is low but increased from 318 in 2005 to 606 in 2010 (▶ Tab. 1) showing a disproportional increase of PEs in women. Stratifying PE cases according to the presence (I26.09) or absence (I26.9) of acute cor pulmonale, the increase in the young females is especially marked in PE without acute cor pulmonale (▶ Fig. 2). The gender-specific difference is highest in the group at the ages of 16–17 and 18–19 years and gradually declines until the age of 32 to 33 years (▶ Fig. 3).

For DVT we could not show comparable changes over time. The total number of young people hospitalised for DVT did not show any trend, and the difference in numbers between males and females varied from 449 to 606. The data were even less specific concerning deep vein thrombosis of lower extremity (I80.1-I80.3) only.

Discussion

The presented data taken from the German DRG statistics show a disproportionately higher increase of young female patients hospitalized for PE as principal diagnosis in the recent years. Such a trend could not be shown for hospitalisation due to DVT. But as most of DVT patients are treated in an outpatient setting in Germany in the recent years hospitalized DVT patients are not necessarily representative for the whole

Statistics

Detailed lists of all PEs and DVTs documented in patients aged 10 to 39 years were provided by the Federal Statistical Office. Cases were divided into those with PE

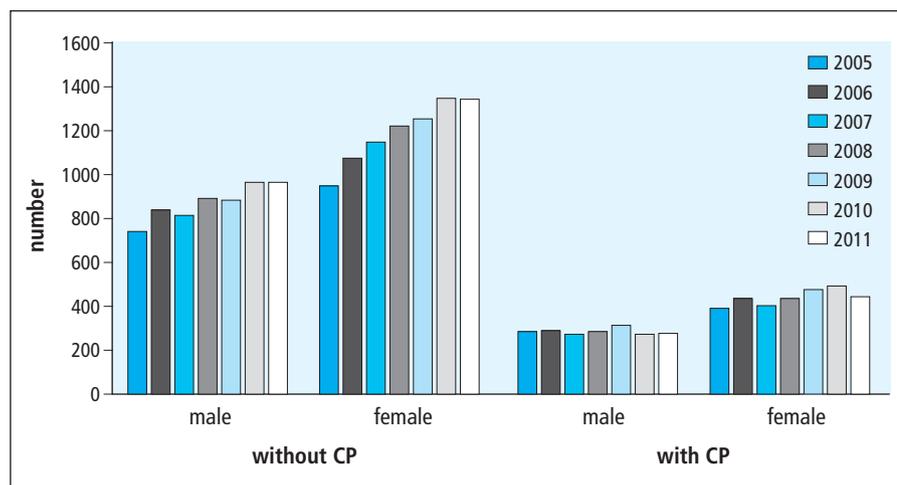


Fig. 2 Absolute numbers of patients with PEs with acute cor pulmonale (CP) (ICD code I26.0) and those without acute CP (ICD codes I26.9) documented as principal diagnosis in the years 2005 to 2011 separated for male and female patients aged 10 to 39 years.

group of patients suffering from DVT. On the other hand there is no trend to treat symptomatic PE in an outpatient setting.

We do not really know what causes the increase in young females hospitalised for PE up to 2010 and the decrease in 2011. PE and DVT in young people can be supposed to be a multi causal disease with changing impact of risk factors in different age groups. Pregnancy and oral contraception but also trauma, venous compression syndromes, inflammatory bowel disease and intravenous drug abuse have been reported to be typical risk factors in such a young population we describe. Even intravenous drug abuse can reach up to 7% of all lower limb DVTs in specific areas (10). We could not support these findings in our prior analysis (6). Pregnancy, inflammatory bowel disease and intravenous drug abuse summed up to around 10% only. Injury and toxicities were only slightly more frequent in males. The systematic analysis of all documented diagnosis suggests that clinical manifestation of PE in men is different from that in women. A much higher rate of males have documented thrombosis and pneumonia and we did not know why females have less. Older registries already reported that use of oral contraceptives compared to malignancy, pregnancy or immobilization is associated with a higher number of patients presenting with PE only (4). The lack of documented DVT in almost half of the young females in Germany should raise some concerns. If DVTs were not present and there was no lack of documentation this point could be an indirect hint onto the impact of oral contraceptives. On the other hand venous thrombosis of the pelvic veins has to be assumed as a source for PE in these patients. In case of DVT evaluation by means of compression ultrasound or phlebography venous thrombosis of the internal iliac vein were not excluded (11).

Unfortunately the use of COCs is not documented within the DRG system. It would be very easy to do. We (the authors) contacted the German Ministry of Health and made an enquiry in 2011. It would be easy to obtain data on the use of COCs in young females with PE as the principal diagnosis from hospitals. Doing so could provide an interesting insight into the impact of

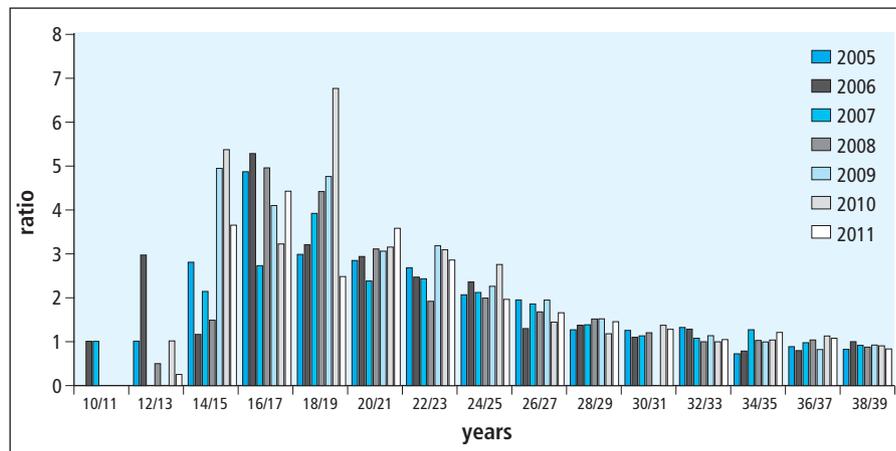


Fig. 3 Ratio of female and male patients (number of females divided by number of males) with PE as principal diagnosis in the years 2005 to 2011 separated in two year age groups

COCs on PE in Germany. We hypothesize that the decrease in hospitalised females suffering from PE in 2011 could even be already constitute an effect of a change in the use of fourth-generation COCs, in that less thrombogenic contraceptives were prescribed.

The higher increase in PE without and with acute cor pulmonale is striking. It is unclear whether some COCs differ in their spectrum of VTE or whether a higher awareness of PE could encourage the doctors to send more women with unspecific symptoms for diagnosis.

Limitations

Although routine data in the electronic patient record is frequently used for secondary purposes, there is currently no systematic analysis of coding quality in Germany (9). Whether coding matches reality as a prerequisite for further use of the data in medicine and health politics has to be investigated in controlled trials. Thus, we cannot estimate the rate of wrong coding of PE.

As the choice of primary diagnosis is on the physician's own authority and strongly affects the reimbursement in the German DRG system, one might be motivated to replace PE as primary diagnosis with other additional diagnoses and vice versa. Therefore, we recommend further health economic studies to quantify the effects and incentives of up-coding in the treatment of PEs in Germany.

It should be pointed out that the analysis is based on cases and not on individual patients. As a consequence, a patient may be included several times in the statistics if he had recurrent events at different times within one year. We also could not separate provoked from spontaneous events.

Comparison of the presented data with other studies has to consider differences in study populations as well as the uncertainty about the diagnosis PE. Often PE is diagnosed by indirect criteria without objective tests.

ICD codes describing thrombosis (I80.0; 80.1; 80.2; 80.3; 80.8; 80.9) covers a wide spectrum of venous disease including DVT as well as superficial vein thrombosis. Thus the given figures do not necessarily represent DVT only.

Conclusion

The presented data derived from the German DRG-Statistic show a dysproportional higher increase of young women hospitalised for pulmonary embolism as principal diagnosis in the recent years. The possible impact of oral contraception for this increase has to be further elucidated.

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Conflict of interest

No fundings received; the authors declare that they have no conflict of interest.

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