Chest radiography and abdominal ultrasound in general practice

Anouk Mariëlle Speets

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Promotores

Prof. dr. W.P.Th.M. Mali
Department of Radiology
University Medical Centre Utrecht, The Netherlands

Prof. dr. A.W. Hoes
Julius Centre for Health Sciences and Primary Care
University Medical Centre Utrecht, The Netherlands

Prof. dr. Y. van der Graaf
Julius Centre for Health Sciences and Primary Care
University Medical Centre Utrecht, The Netherlands

Co-promotor

Dr. S. Kalmijn
Julius Centre for Health Sciences and Primary Care
University Medical Centre Utrecht, The Netherlands

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Voor Hans en Milica
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CHAPTER 2

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CHAPTER 3

Speets AM, Van der Graaf Y, Hoes AW, Kalmijn S, Sachs APE, Rutten MJCM, Gratama JWC, Montauban van Swijndregt AD, Mali WPThM. Chest radiography in general practice: indications, diagnostic yield, and consequences for patient management. Submitted.

CHAPTER 4

Speets AM, Hoes AW, Van der Graaf Y, Kalmijn S, Sachs APE, Mali WPThM. Chest radiography in patients suspected of pneumonia in primary care: diagnostic yield, and consequences for patient management. In revision for Eur Respir J.

CHAPTER 5

Speets AM, Kalmijn S, Hoes AW, Van der Graaf Y, Mali WPThM. The yield of abdominal ultrasound in patients with abdominal pain referred by general practitioners. Submitted.

CHAPTER 6

Speets AM, Hoes AW, Van der Graaf Y, Kalmijn S, De Wit NJ, Montauban van Swijndregt AD, Gratama JWC, Rutten MJCM, Mali WPThM. Upper abdominal ultrasound in general practice: indications, diagnostic yield, and consequences for patient management. In revision for Fam Pract.

CHAPTER 7

Speets AM, Van der Graaf Y, Hoes AW, Kalmijn S, De Wit NJ, Mali WPThM. Expected and unexpected gallstones in primary care. Submitted.

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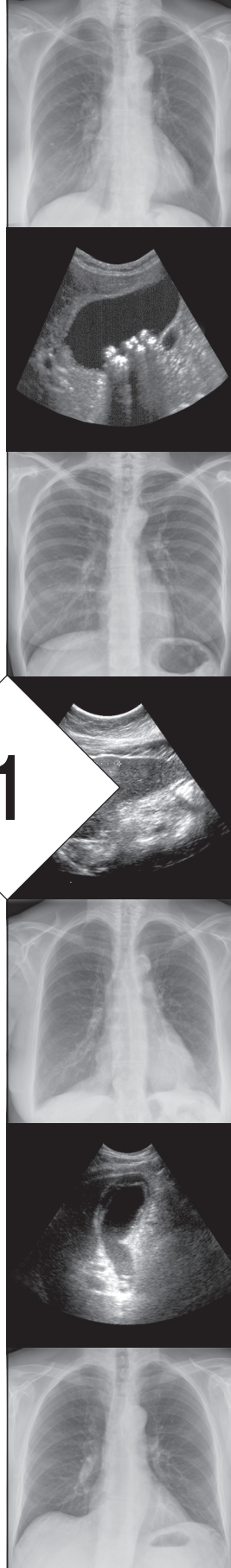
Introduction



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The diagnostic process is a multivariable and consecutive process of estimating the diagnostic probability of the presence of a particular disease given combinations of test results. A diagnosis in clinical practice starts with obtaining basic information of patients (e.g. age, gender and medical history), followed by history taking and physical examination and, if necessary, by more invasive, patient burdening, time consuming and costly tests, such as laboratory or imaging investigations.[1,2] The main goal of a radiological examination is to provide information on the presence or absence and nature of a certain disease. In addition, the course of a disease can be followed, by demonstration of the disease process itself or the effects of the disease process on the normal anatomy.[3] This thesis focuses on the first goal: the diagnostic value of imaging examinations. A valuable diagnostic investigation can be defined as one in which the result will either alter the anticipated patient management or increase confidence in the clinician's diagnosis.[4,5] In addition, diagnostic investigations can be very valuable for a patient's uncertainty.

Chest radiography (CXR) and abdominal ultrasound (US) are two of the most widely used diagnostic imaging techniques in Western societies. CXR is an important method for evaluation of the lower airways, pulmonary parenchyma and vessels, mediastinum, heart, pleura and chest wall.[6] Diagnostic indications are signs and symptoms potentially related to the respiratory, cardiovascular, upper gastrointestinal, and musculoskeletal system, evaluating diseases involving the thorax, and the staging of extrathoracic as well as intrathoracic tumors.[6] CXR is considered the reference standard for diagnosing pneumonia.[7-10] In Western societies, on average 236 CXRs per 1000 patients per year are performed and this technique accounts for 25% of the annual total number of diagnostic imaging procedures. The corresponding numbers for The Netherlands are 120 CXRs per 1000 patients per year, and they comprise 20% of all diagnostic imaging procedures.[11] In The Netherlands, approximately one quarter of all CXRs are requested by general practitioners (GPs).

Abdominal US is important for the evaluation of many structures in the abdomen, such as the liver, gallbladder, biliary tract, pancreas, aorta and kidneys. Indications include abdominal, flank and/or back pain, palpable abnormalities, abnormal laboratory values suggestive for abdominal pathology, follow-up of known or suspected abnormalities and search for metastatic disease or occult primary disease.[12] Abdominal US is an important diagnostic imaging method for detecting gallstones, providing more than 95% sensitivity and specificity for the diagnosis of gallstones greater than 2 mm in diameter.[13-15] Annually, about 200,000 abdominal US are requested by GPs in The Netherlands; approximately 40% of all requested US.

The frequency with which even these relatively inexpensive and non-invasive diagnostic tests are performed clearly places a burden on health care. GPs in The Netherlands annually request approximately 500,000 CXRs and 200,000 abdominal US, amounting to 35 million euros per year. Furthermore, it is important to keep in mind that CXR and abdominal US are used for a broad range of indications, and that the positive and negative predictive values (and sensitivity and specificity) are not 100%. This results in patients with a positive test result who do not have a disease (i.e. false positives), and patients with a disease not detected with the diagnostic test (i.e. false negatives), which can lead to, respectively, redundant treatments or unjustified reassurance of the patient. Besides, unnecessary diagnostic investigations may lead to incidental findings, or to additional unnecessary diagnostic procedures (e.g. a more costly CT-scan or MRI). All these factors can multiply the costs of a, at first sight, relatively inexpensive and simple diagnostic test. Therefore it is important that their diagnostic value in current clinical practice is assessed.

Little is known on the diagnostic yield of CXR and abdominal US in patients referred by GPs, even on the most frequently used indications for these two radiologic investigations, i.e. patients suspected of pneumonia or of cholelithiasis. In particular, there is insufficient knowledge of the exact frequencies and time trend of referrals for CXR and abdominal US, its diagnostic value in terms of changes in patient management decisions in primary care, and the value for the patients themselves. We are aware of only two large studies[16,17] on CXR in patients referred by GPs, and four retrospective studies[18-21] that examined abdominal complaints and referral by GPs for abdominal US. The studies of Guyer et al[16] and Keogan et al[17] reported clinically relevant abnormalities in 21% and 23% of patients referred for CXR by GPs, respectively. The percentages of clinically relevant abnormalities detected on abdominal US ranged from 25% to 30%.[18-21] Clearly, however, the full value of these diagnostic imaging techniques cannot be assessed in terms of positive findings alone. Firstly, the relevance of detected abnormalities must be assessed with respect to clinical practice, because positive findings may be incidental and without any consequences. Positive findings are relevant primarily when they result in changes of anticipated patient management. On the other hand, negative examinations can also have great potential value, notably in reassuring the patient. Neither of these studies however cited both positive and negative findings in detail, nor assessed the value of CXR or abdominal US in terms of changes in anticipated patient management.

These considerations were the main justifications for the studies described in this thesis. The main objective of this thesis was to determine the clinical effectiveness of CXR and upper abdominal US in general practice. The objectives of the studies presented in the following chapters were:

1. To provide detailed information on the number and time trend of CXRs and abdominal US examinations by age, gender, referring physician and ethnicity in The Netherlands (Chapter 2).
2. To assess the influence of CXR on the change in anticipated patient management in general practice, and to evaluate the consequences of the CXR according to the patient (Chapter 3).
3. To determine the effect of CXR on the probability estimation of pneumonia by GPs, the influence of CXR on patient management, and consequences of CXR according to the patient among primary care patients with a clinical suspicion of pneumonia (Chapter 4).
4. To examine the prevalence and determinants of significant abnormalities on abdominal US in patients with abdominal pain referred by GPs (Chapter 5).
5. To assess the influence of upper abdominal US on the change in anticipated patient management in general practice, and to evaluate the consequences of the abdominal US according to the patient (Chapter 6).
6. To assess the differences in signs and symptoms of primary care patients with expected and unexpected gallstones referred for upper abdominal US (Chapter 7).
7. To outline the difficulties of diagnostic research assessing the value of diagnostic tests that are routinely used in a wide variety of complaints (Chapter 8)

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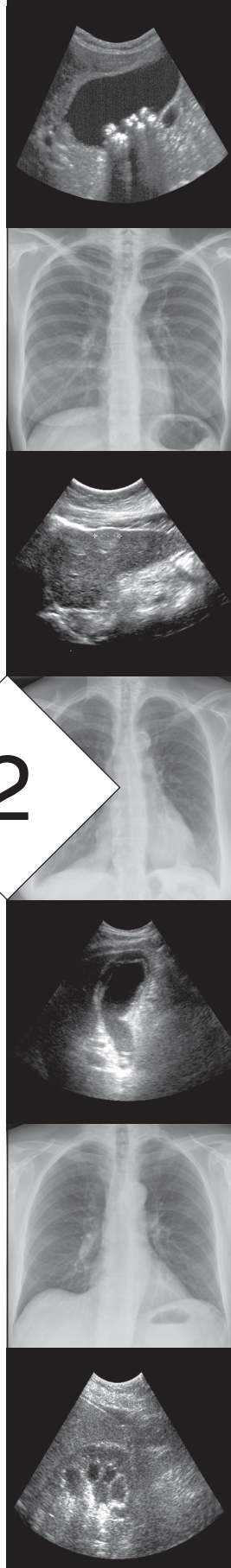
Frequency of chest radiography and abdominal ultrasound in The Netherlands



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Speets AM, Kalmijn S, Hoes AW, Van der Graaf Y, Smeets HM, Mali WPThM. Frequency of chest radiography and abdominal ultrasound in The Netherlands: 1999-2003. Eur J Epidemiol. 2005;20(12):1031-1036.

Abstract

Background. Chest radiography (CXR) and abdominal ultrasound (US) are two widely used diagnostic imaging techniques in Western societies. However, little is known about the frequency of these examinations and its determinants. The aim of this descriptive study was to provide detailed information on the number of CXR and abdominal US examinations by age, gender, referring physician and ethnicity.
Methods. We used data of approximately 3,000,000 sick fund insured persons of the Health Insurance Company Agis in The Netherlands from 1999 to 2003. We calculated annual numbers and corresponding 95% confidence intervals for different age, gender and ethnicity categories.
Results. The mean age of the population was 38±22 years and 46% were male. CXRs were ordered in 130 per 1000 persons per year and abdominal US examinations in 39 per 1000 persons per year; these frequencies did not change noticeable over the five-year period. CXR was performed more often in males (156 versus 109 per 1000 persons/year in females; $p<0.05$) and abdominal US more often in females (43 versus 34 per 1000 persons/year in males; $p<0.05$). Frequencies were highest in persons aged 70-79 years. Compared to medical specialists, general practitioners more frequently referred younger patients and females, especially for abdominal US. Up to the age of 60 years the frequencies of both CXR and abdominal US were higher in Turks and Moroccans compared to other persons.
Conclusion. This study showed marked differences in the frequencies of CXR and abdominal US according to age, gender and ethnicity in The Netherlands.

Introduction

The goal of a radiological examination is to provide information on the presence or absence and nature of a certain disease or to follow its course, in addition to information obtained by the medical history, physical examination and other diagnostic tests.[1] Ideally, there should always be a sufficient clinical suspicion to warrant a radiological examination, and a reasonable anticipation that the results of the imaging test, normal or abnormal, may influence the management of the patient.[2]

There is little scientific literature on the exact frequency of regularly performed radiodiagnostic tests, especially imaging tests requested by general practitioners (GPs). Chest radiography (CXR) and abdominal ultrasound (US) are two of the most widely used diagnostic imaging techniques in Western societies.[2-6] However, the frequency and determinants of CXR and abdominal US examinations are largely unknown. The aim of this descriptive study was to provide detailed information on the number of CXR and abdominal US examinations by age, gender, referring physician and ethnicity in The Netherlands.

Methods

In this study we used information from a large dataset of the Health Insurance Company Agis located in Amersfoort in The Netherlands. In the Agis database all health care procedures of sick fund insured persons are documented in detail. Besides health care procedures, a number of personal characteristics are documented, such as date of birth and gender. Agis refunds only expenses claims after the computer has verified all data of the claim (e.g. name, birth date and address of the patient). Data are submitted to the database after this automated verification, to ensure the validity of these data.

We used information of approximately 3,000,000 sick fund insured persons registered in the Agis database from 1999 to 2003, encompassing almost one-fifth of the Dutch population. Of each registered person, information on gender, date of birth and personal insurance number was extracted. The age and gender distribution of our study population was similar to that of the Dutch population at large (data provided by Statistics Netherlands[7]). Thus, our study population is a good reflection of the population in The Netherlands. All CXRs and abdominal US (including entire abdomen, upper abdominal and lower abdominal US; excluding pregnancy US) that were performed for in- and outpatients were registered. Data included the

TABLE 1. Baseline characteristics of sick fund insured persons: means and percentages 1999-2003

	n (%)
Age	
0-9 years	67,667 (11.4)
10-19 years	62,901 (10.5)
20-29 years	93,850 (15.7)
30-39 years	107,734 (18.1)
40-49 years	80,754 (13.5)
50-59 years	68,033 (11.4)
60-69 years	52,827 (8.9)
70-79 years	39,321 (6.6)
80-89 years	19,651 (3.3)
> 90 years	3,657 (0.6)
Gender	
Male	273,046 (45.8)
Female	323,349 (54.2)
Ethnicity*	
Moroccans	22,247 (3.8)
Turks	14,445 (2.4)
Other	558,798 (93.8)

* Only data of 1999

date of the radiological examination and the referring physician (medical specialist or GP). We could use only the data of 1999 to 2001 for the results on the referring physicians, because Agis changed the coding for the applicants in 2002. In addition, Agis determined the ethnicity of Moroccan and Turkish people of all insured persons in 1999, based on the nationality of the first generation Moroccan and Turkish people and subsequently a match of their names with the remaining insured persons.[8] This way we were able to investigate whether the frequency of CXRs and abdominal US among Moroccans and Turks was different from the frequency among other insured persons in 1999.

We calculated the frequencies of CXR and abdominal US per year by age, gender and ethnicity. Because of the large differences between the age groups, the frequencies per 1000 persons per year for gender and ethnicity were standardized for age.[9] The distribution of the ten age groups of all insured persons in 1999 were handled as reference group. This way, trends in time would still be detectable. We calculated 95% confidence intervals for the frequencies. Differences between frequencies were considered significant when the confidence intervals did not overlap.[9]

TABLE 2. Mean frequency (per 1000 persons/year) by age groups and gender: chest radiography and abdominal ultrasound 1999-2003

	Chest radiography	Abdominal ultrasound
Age		
0-9 years	41.5	15.6
10-19 years	20.3	11.1
20-29 years	35.4	20.1
30-39 years	54.0	28.6
40-49 years	98.5	41.2†
50-59 years	176.2	55.5
60-69 years	307.6	75.1†
70-79 years	475.1	91.5
80-89 years	427.0	77.2†
> 90 years	268.1	43.2†
Gender*		
Male	155.6	33.5
Female	108.9	42.9

* Standardized for age

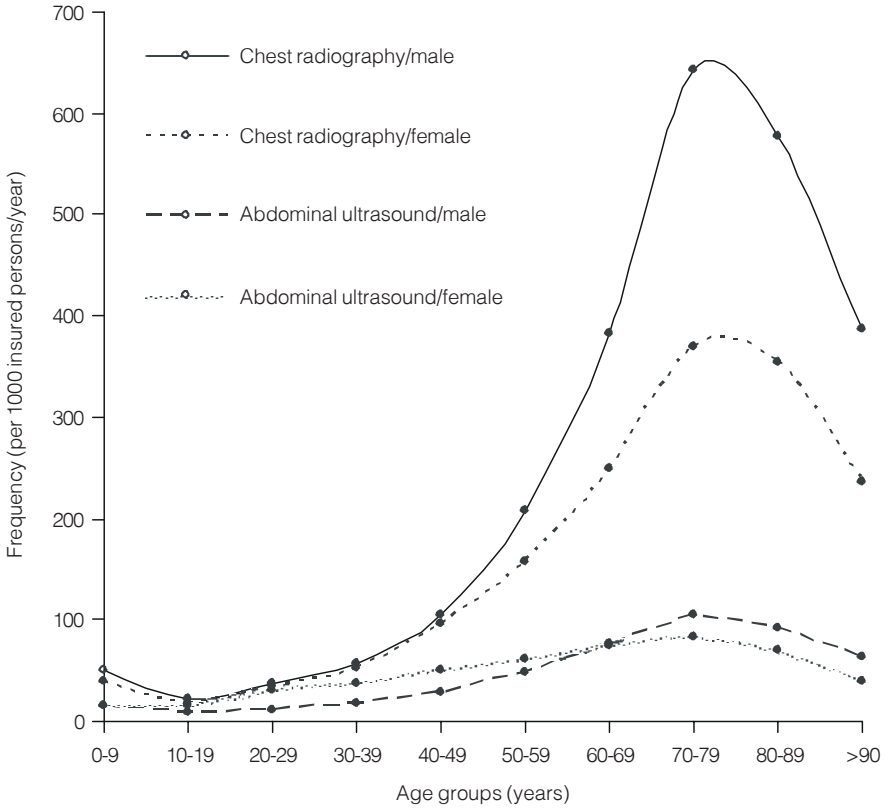
† p>0.05 for difference in frequency of abdominal ultrasound in persons aged 40-49 years compared to those aged >90 years, and in persons aged 60-69 compared to those aged 80-89 years; all other differences between frequencies were statistically significant (95% confidence intervals did not overlap)

Results

The mean number of sick fund insured persons from 1999 to 2003 was 596,395 per year, 46% was male and the mean age was 38 years (SD 22 years). The age distribution is shown in Table 1. In 1999 4% of the sick fund insured persons were of Moroccan and 2% of Turkish origin.

Differences of CXR and abdominal US frequencies between 1999 and 2003 were minimal (p>0.05). Consequently, only mean numbers per 1000 persons of these 5 years combined are shown in the tables and figure. The number of ordered CXRs ranged from 20 (95% CI 19.2-21.4) per 1000 persons per year in the 10-19 years age group to 475 (95% CI 468.3-481.9) per 1000 persons per year in the group aged 70 to 79 years. Corresponding numbers for abdominal US were 11 (95% CI 10.3-11.9) and 92 (95% CI 88.5-94.5) examinations per 1000 persons per year for the two same age groups (Table 2). On average, CXR was performed significantly more often in males and abdominal US significantly more often in females (Table 2). Figure 1 shows the relation of CXR and abdominal US frequencies between gender and the ten age groups. Gender differences for CXR are very

FIGURE 1. Mean frequency (per 1000 persons/year) by age groups and gender: chest radiography and abdominal ultrasound 1999-2003



small till the age of 50 years; the increase in frequency in persons aged 50 years and older was much larger in males. The frequency of abdominal US was higher in females aged 0-70 years, and males of 70 years and older. For CXR, as well as abdominal US, a marked decline in the number of examinations occurred after the age of 80 years.

On average 73% of the patients undergoing CXR were referred by a medical specialist and 24% by their GP. Numbers for abdominal US were 58% and 39% respectively (Table 3). Medical specialists more frequently referred patients twice or more often per year than GPs, but overall the number of multiple examinations was much smaller in the abdominal US group than in the CXR group. This table

TABLE 3. Mean numbers and percentages for requests made by medical specialists and general practitioners: chest radiography and abdominal ultrasound 1999-2001

		Chest radiography		Abdominal ultrasound	
		Medical specialist n (%)	General practitioner n (%)	Medical specialist n (%)	General practitioner n (%)
Referrals*		56,039 (73.3)	18,502 (24.2)	13,213 (57.8)	8,955 (39.1)
Number of	1	20,616 (70.2)	14,327 (89.9)	9,749 (87.0)	8,056 (95.0)
examinations	2	4,128 (14.1)	1,237 (7.8)	1,105 (11.2)	386 (7.7)
per insured	3	1,634 (5.6)	217 (1.3)	237 (2.1)	24 (0.3)
person	4	890 (3.0)	59 (0.4)	72 (0.6)	7 (0.1)
	>4	2,112 (7.1)	92 (0.6)	44 (0.4)	5 (0.1)
Age					
0-9 years		1,967 (3.5)	935 (5.0)	854 (6.5)	216 (2.4)
10-19 years		802 (1.4)	473 (2.6)	419 (3.2)†	250 (2.8)†
20-29 years		2,103 (3.8)	1,308 (7.1)	898 (6.8)	1,046 (11.7)
30-39 years		3,447 (6.1)	2,352 (12.7)	1,306 (9.9)	1,698 (18.9)
40-49 years		5,049 (9.0)	2,716 (14.7)	1,527 (11.6)	1,701 (19.0)
50-59 years		8,253 (14.7)	3,295 (17.8)	2,087 (15.8)	1,527 (17.1)
60-69 years		12,244 (21.8)	3,400 (18.4)	2,478 (18.8)	1,268 (14.1)
70-79 years		14,750 (26.3)	2,781 (15.0)	2,464 (18.7)	866 (9.7)
80-89 years		6,660 (11.9)	1,119 (6.0)	1,075 (8.1)	342 (3.8)
> 90 years		761 (1.4)	124 (0.7)	104 (0.8)	42 (0.5)
Gender					
Male		28,571 (51.0)	8,746 (47.3)	5,619 (42.5)	2,584 (28.9)
Female		27,467 (49.0)	9,756 (52.7)	7,594 (57.5)	6,370 (71.1)

* Percentages do not add up to 100%: remaining percentages were unknown referring physicians
† P>0.05; all other differences between the frequency of chest radiography and abdominal ultrasound examinations ordered by medical specialists and GPs were statistically significant (95% confidence intervals did not overlap)

also illustrates that GPs more often referred younger patients and females, especially for abdominal US. Compared to other insured persons Moroccans and Turks were referred more frequently by GPs than medical specialists (Table 4).

In both males and females abdominal US was performed significantly more often in Moroccans and Turks than in other persons. Compared to the other insured persons the frequency of CXR was only higher for Moroccan females ($p<0.05$), but lower for Moroccan males and all Turkish people ($p<0.05$). Up to the age of 60 years the frequencies of both radiological examinations were higher for Turks and Moroccans and significant in most age groups (Table 4).

TABLE 4. Mean numbers and percentages for requests made by medical specialists and general practitioners, and frequency (per 1000 insured persons/year) of Moroccan, Turkish and other persons according to age and gender: chest radiography and abdominal ultrasound 1999

	Chest radiography			Abdominal ultrasound		
	Moroccans	Turks	Other	Moroccans	Turks	Other
Referrals n (%)*						
Medical specialist	1,011	795	54,379	360	282	12,545
	(53.8)	(58.0)	(73.4)	(38.7)	(46.8)	(58.3)
General practitioner	831	540	17,398	551	308	8,102
	(44.2)	(39.4)	(23.5)	(59.2)	(51.1)	(37.7)
Frequency per 1000 persons/year						
Age						
0-9 years	61.4	65.3	43.4	18.7‡	19.3‡	15.7
10-19 years	26.0‡	23.1‡	21.7	9.0‡	14.1‡	11.0
20-29 years	53.4	96.2	35.3	42.1	45.7	20.0
30-39 years	93.4	109.2	52.5	62.4	68.3	26.5
40-49 years	146.5	185.1	100.2	101.4	79.5	39.9
50-59 years	251.0	213.3	173.8	110.4	96.1	54.1
>60 years	293.6	209.9	390.7	89.4‡	44.1	80.8
Gender†						
Male	136.6	148.9	158.9	38.9	41.2	32.9
Female	121.5	81.7	109.3	93.4	68.5	42.3

* Percentages do not add up to 100%: remaining percentages were unknown referring physicians
† Standardized for age
‡ p>0.05 compared to the category "other" (i.e. non-Moroccan and non-Turkish persons); all other differences between the frequency of chest radiography and abdominal ultrasound examinations in Moroccans and Turks compared to the category "other" were statistically significant

Discussion

In the period 1999 to 2003, CXRs were ordered in 130 per 1000 persons per year in The Netherlands and abdominal US in 39 per 1000 persons per year. The frequencies were more or less constant over the years. This study showed marked differences in the frequencies of CXR and abdominal US according to age, gender and ethnicity in The Netherlands. Since populations and standard of living in countries in North-West Europe are quite comparable, our findings seem generalizable to other countries in North-West Europe, albeit that the referral rates for these examinations by primary care physicians are only relevant for countries with a similar, primary care-based health care system, such as England and Sweden. We found two studies that published numbers of CXR in The Netherlands.[4,5] To the best of our knowledge,

there is no scientific literature on annual numbers of abdominal US, so it is not possible to compare the numbers of our study with those of other studies.

The United Nations Scientific Committee on the Effects of Atomic Radiation regularly monitored the medical use of radiation. Their most recent report was published in 2001.[4] The mean annual number of CXR examinations from 1991-1996 in The Netherlands was 120 per 1000 population and CXR contributed 20% to the annual total numbers of diagnostic research. The mean frequency of 130 CXRs per 1000 persons per year in our study is somewhat higher.

Beentjes and Timmermans published numbers for the distribution of age and gender of patients undergoing CXR in The Netherlands in the period 1984-1985.[5] The shape of their age distribution corresponds well with our figures. The number of CXRs for males was 171 per 1000 males and 142 per 1000 females. The annual numbers in our study are lower, 156 and 109 per 1000 sick fund insured persons, respectively. The long period of almost 20 years may explain part of this difference in prevalence, such as the development of new alternative diagnostic imaging techniques (e.g. CT-scan).

Before discussing the differences in frequencies of CXR and abdominal US found in our study we emphasize that many factors (e.g. psychological and economical) may have influenced the observed differences. It is beyond the scope of this study to thoroughly investigate all causes for these differences. Further studies, including more detailed information on relevant determinants, are needed to explain the observed differences in frequencies.

The larger annual numbers of CXR in males could be partly explained by the higher frequency of smoking and a higher prevalence of more severe lung diseases, such as lung carcinoma and chronic obstructive pulmonary disease, in the male population.[10-12] However, trends in the prevalence of cigarette smoking are declining among males and increasing among females and concurrently opposite trends are observed for lung diseases.[10-12] This could be a reason for the smaller gender differences in the younger age groups. Females more often have abdominal complaints, can suffer from gynecological problems and the prevalence of abdominal diseases, such as infectious gastrointestinal diseases, is higher.[15,16] One of the determinants for the higher frequency of abdominal US in males aged 70 years and older could be the frequency of abdominal aortic aneurysms (AAA), because male gender and increasing age are important risk factors for AAA.[13,14] AAA is ten times more common in 65- to 75-year-old men compared to women of the same age.[13] A marked decline in the number of CXR and abdominal US examinations occurred after the age of 80 years. One can only speculate on the underlying reasons. Perhaps the number of examinations is low because patient management

is unlikely to change in these very old people or because the patient burden is too high. Further research is required to address this issue.

Up to the age of 60 years both CXR and abdominal US were ordered more frequently in Turks and Moroccans compared to other persons. A community survey among the Amsterdam population showed that Moroccan and Turkish persons reported a poorer personal health and higher use of health care compared to the indigenous population of the same age and gender.[17] Data of the Dutch National Survey on Morbidity and Interventions in General Practice showed that the frequency of gastrointestinal and lung diseases was higher for Moroccans and Turks in comparison to the Dutch population.[18] Possible explanations for the higher frequency of health problems in the Moroccan and Turkish population in The Netherlands are adverse social and economic position of ethnic minority groups, differences in congenital predisposition, cultural factors, living conditions and diet.[8,17,18] Furthermore, communication problems could result in a higher referral frequency of Moroccans and Turks by GPs for CXR and abdominal US shown in this study.[8,17,18]

As expected, medical specialists more frequently referred patients for two or more examinations per year than GPs. The number of multiple examinations was much smaller in the abdominal US group than in the CXR group. In The Netherlands, routine radiological investigations, such as CXR, are performed often when patients are submitted to the hospital. Each patient at the intensive care ward is daily examined with CXR and this increases the number of multiple CXRs requested by medical specialists.

In conclusion, in the period 1999 to 2003 CXRs were ordered in 130 per 1000 persons per year and abdominal US in 39 per 1000 persons per year in The Netherlands. These frequencies did not change noticeable over the five-year period. This study showed marked differences in the frequencies of these examinations according to age, gender and ethnicity.

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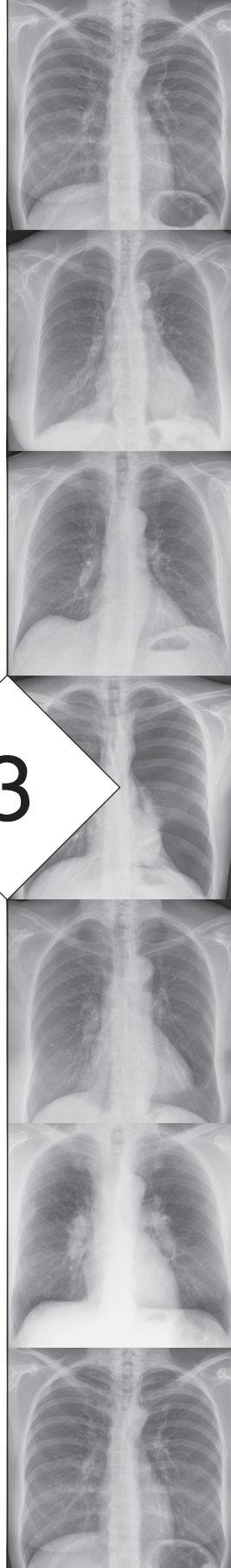
Indications and consequences of chest radiography in general practice



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Speets AM, Van der Graaf Y, Hoes AW, Kalmijn S, Sachs APE, Rutten MJCM, Gratama JWC, Montauban van Swijndregt AD, Mali WPThM. Chest radiography in general practice: indications, diagnostic yield, and consequences for patient management. Submitted.

Abstract

Background. Chest radiography (CXR) is frequently performed in Western societies. There is insufficient knowledge of its diagnostic value in terms of changes in patient management decisions in primary care. The aim of this study was to assess the influence of CXR on patient management in general practice.

Methods. 792 patients aged ≥ 18 years were referred by 78 general practitioners (GPs) for CXR to one of the three participating hospitals in The Netherlands. The main outcome was change in patient management assessed by means of questionnaires filled in by GPs before and after CXR.

Results. Mean age of the patients was 57.3±16.2 years, 53% were male. Clinically relevant abnormalities were found in 24% of the CXRs. Patient management changed in 60% of the patients following CXR. Main changes included: fewer referrals to a medical specialist (from 26% to 12%); reduction in initiation or change in therapy (from 24% to 15%); and more frequent reassurance (from 25% to 46%). However, this reassurance was not perceived as such in a quarter of these patients. A change in patient management occurred significant more frequently in patients with complaints of cough (67%), exhibited abnormalities during physical examination (69%), or a suspected diagnosis of pneumonia (68%).

Conclusion. Patient management by the GP changed in 60% of patients following CXR. CXR substantially reduced the number of referrals and initiation or change in therapy, and more patients were reassured by their GP. Thus, CXR seems to reduce the burden on patients and health care.

Introduction

Chest radiography (CXR) is an important diagnostic method for evaluation of the airways, pulmonary parenchyma and vessels, mediastinum, heart, pleura and chest wall.[1] It is one of the most widely used diagnostic imaging techniques in Western societies; on average 236 CXRs per 1000 patients per year are performed and this technique accounts for 25% of the annual total number of diagnostic imaging procedures.[2] The corresponding numbers for The Netherlands and the United Kingdom are 120 (20%), and 141 (29%) CXRs per 1000 patients per year, respectively.[2] In The Netherlands, approximately one quarter of the CXRs are requested by GPs.

The frequency with which even relatively inexpensive and non-invasive diagnostic tests are performed clearly places a burden on health care. Therefore it is important that their influence on patient management is assessed. Unnecessary diagnostic investigations may lead to incidental findings, or to additional unnecessary diagnostic procedures or even over treatment.

A valuable diagnostic investigation can be defined as one in which the result will either alter management or increase confidence in the clinician's diagnosis.[3,4] Current guidelines for CXR are aimed mainly at diseases instead of at the complaints with which patients present themselves.[1,3,5-8] CXR in patients referred by GPs has received little attention in the scientific literature. There is insufficient knowledge of its diagnostic value in terms of changes in patient management decisions in primary care. We are aware of only two large studies on CXR in patients referred by GPs. The studies of Guyer et al[9] and Keogan et al[10] reported clinically relevant abnormalities in 21% and 23% of patients referred for CXR by GPs, respectively. Clearly, the full value of CXR cannot be assessed in terms of positive findings alone. Firstly, the relevance of detected abnormalities must be assessed with respect to clinical practice, because positive findings may be incidental and without any consequences. Positive findings are relevant only when they result in changes of patient management. On the other hand, negative examinations can also have potential value when they result in changes of patient management and can be very helpful in reassuring the patient. Neither of these studies however cited both positive and negative findings in detail, nor assessed the value of CXR in terms of changes in patient management. Also, the consequences of CXR according to the patient were not studied before.

The objective of this study was to assess the influence of both positive and negative findings of CXR on the change in patient management in general practice and to evaluate the consequences of the CXR according to the patient.

Methods

This prospective cohort study was conducted from April 2003 to December 2004. In total, 78 GPs in the catchment area of one of three participating general hospitals located in three main cities in The Netherlands (Jeroen Bosch Hospital in 's-Hertogenbosch; Gelre Hospitals in Apeldoorn; 'Onze Lieve Vrouwe Gasthuis' in Amsterdam) were involved. 28 GPs (36%) worked in a solo practice, 58 (74%) were male, 40 GPs (51%) graduated between 1968-1980, 19 (24%) between 1980-1990, and 19 (24%) between 1990-1997. All patients of 18 years and older who were referred for CXR (posteroanterior and lateral view) by their GP to one of these hospitals were included in the study. The patients received an exclusion form from their GP, which they could return to the study coordinator if we were not allowed to use their data for this study. The study was approved by the Medical Ethics Review Board.

All GPs were asked to fill in a standardized form before requesting a CXR, including information on history, physical examination, indication, suspected diagnosis, and proposed patient management. The anticipated patient management was filled in as if no CXR would be performed. The management options included: referral to a medical specialist; initiation or change in therapy; reassurance of the patient; and follow-up by the GP (watchful waiting or additional diagnostic testing). The GP could choose only one of these management options. After the GP received the report (within 1-4 days after the CXR) he or she filled in a second questionnaire; again including the suspected diagnosis and anticipated patient management plan.

The reports of CXR were collected in the three hospitals to determine the findings of CXR. These findings were categorized into six groups: (1) malignancy; (2) pneumonia; (3) COPD/asthma/chronic bronchitis; (4) other clinically relevant abnormalities (heart failure and unclear abnormalities that required further investigation according to the radiologist); (5) the follow-up of abnormalities detected previously on CXR; (6) no abnormality. The first four groups were considered clinically relevant abnormalities.

Six months after the CXR a short questionnaire was sent to all patients, in order to assess the consequences of CXR according to the patient (response rate 79%). They could choose one of the following options: definite diagnosis; better treatment; reassurance; nothing; or other. With this information we could check whether reassurance of the patient as reported by the GP was really perceived as reassurance by the patient.

In total 870 patients of 18 years or older were referred for CXR. Patient management plans for 78 patients (9%) were not filled in by the GP before and/or after CXR. These patients were excluded from the study, resulting in a study population of 792 patients. Their patient characteristics were comparable with the included patients.

The primary outcome measure for our study was the proportion of patients in whom there was a change in patient management by the GP following CXR. This proportion and the corresponding 95% confidence interval were calculated using the statistical program Confidence Interval Analysis.[11] Additionally, subgroup analyses were performed to assess whether the patient and GP characteristics influenced the proportion of change in patient management. Associations were tested with chi-squared tests and regarded as significant when the p-value was ≤ 0.05. Data were analysed using SPSS for Windows version 11.0.

Results

The mean age of the patients at time of CXR was 57.3 years (sd 16.2) and 53% were male. Fifty percent of the patients had a history of cough and 25% of dyspnoea. Abnormalities with physical examination were found in 40% of the patients. The most common suspected diagnosis was pneumonia (24%) and malignancy (18%) (Table 1).

The radiology reports of CXR showed no abnormality in 416 patients (53%) and follow-up of an abnormality detected previously on CXR in 179 patients (23%). Clinically relevant abnormalities were found in 197 CXRs (25%), these included: malignancy (n=11; 1%); pneumonia (n=44; 5%); COPD/asthma/chronic bronchitis (n=99; 13%); and other clinically relevant abnormalities that required further investigation according to the radiologist (n=43; 5%). As expected, all patients with a malignancy were referred to medical specialists after CXR, with the exception of one patient, in this case the GP wanted to wait for the results of the additional CT-scan before further action. Patients with pneumonia were mainly treated by the GP with a prescription of antibiotics. Noticeable was that 29 patients (4%) with no abnormalities detected on CXR were referred to a medical specialist. Fifteen patients had unclear complaints that needed further examination, in nine patients lung pathology was excluded and these patients were referred to another medical specialist, e.g. cardiologist. In four patients a clinically relevant abnormality was found with another examination (e.g. abdominal ultrasound), and CXR was used as a screening tool in one patient.

TABLE 1. Patient characteristics (n=792)

	n (%)
Age (mean ± sd in years)	57.3±16.2
Gender (male)	423 (53)
Prior diagnoses	
Malignancy (various locations n=29; lung n=9)	38 (5)
Cardiovascular	95 (12)
Pneumonia	76 (10)
COPD/asthma/chronic bronchitis	143 (18)
History taking	
Smoking	142 (18)
Pain	172 (22)
Respiratory complaints	
Haemoptysis	53 (7)
Cough	394 (50)
Dyspnoea	99 (25)
Other symptoms of respiratory infection*	117 (15)
General complaints	
Weight loss	31 (4)
Fever	53 (7)
General malaise	101 (13)
Abnormalities during physical examination†	317 (40)
Suspected diagnosis pneumonia according to GP	193 (24)
Suspected diagnosis malignancy according to GP	142 (18)

* Abnormal sputum, nasal congestion, throat symptoms, and complaints of a cold
† A physical examination was considered abnormal when abnormalities were detected with auscultation (e.g. wheeze), percussion (e.g. dullness), or palpation (e.g. pain)

The proportion of patients in whom CXR resulted in a change in patient management was 60% (95% confidence interval 57%-64%). Main changes in patient management plans after CXR included: a reduction in anticipated referrals to a medical specialist from 203 (26%) to 97 (12%); a reduction in the number of patients with initiation or change in therapy from 187 (24%) to 119 (15%), which was demonstrated mainly by a reduction in the anticipated prescription of drugs such as antibiotics; and more frequent reassurance of the patient, from 195 (25%) to 363 (46%) patients (Table 2).

Subgroup analyses revealed that the proportion of patients in whom patient management changed after CXR was significantly higher among patients with complaints of cough (67%), exhibited abnormalities during physical examination

TABLE 2. Patient management plans of general practitioners before and after chest radiography n (%)

BEFORE(n) / AFTER (n (%))	Referral medical specialist	Therapeutic management	Reassurance	Follow-up by GP*	Total
Referral medical specialist	**48 (24)**	22 (12)	8 (4)	19 (9)	97† (12)
Therapeutic management	29 (14)	**45 (24)**	15 **(8)**	30 (14)	119† (15)
Reassurance	89 (44)	57 (30)	**141 (72)**	76 (37)	363† (46)
Follow-up by GP*	37 (18)	63 (34)	31 (16)	**82 (40)**	213 (27)
Total	203 (26)	187 (24)	195 (25)	207 (26)	792

* Follow-up by GP: predominantly watchful waiting or additional diagnostic testing, such as spirometry or laboratory investigation

† The differences in proportions of patient management after chest radiography were significant with a p-value ≤ 0.05

(69%) or a suspected diagnosis of pneumonia (68%) (Table 3). The characteristics of the GPs (solo or group practice, gender and year of graduation) had little influence on the proportion of change in management of 60%.

Almost one-fifth of the patients who returned the questionnaire reported that CXR had no consequences, and approximately 50% of the patients were reassured after CXR. It was noted that a quarter of the 363 patients who were reportedly reassured by their GP after CXR failed to perceive the result of the CXR as reassurance.

Discussion

The proportion of patients for whom patient management changed following CXR was 60%. Main changes included: fewer referrals to a medical specialist (from 26% to 12%); a reduction in the number of patients with initiation or change in

TABLE 3. Proportion of changes in patient management after chest radiography in relevant subgroups

	Change in management	
	n	%
All patients	476	60
Age		
< 60 years	249	59
≥ 60 years	227	61
Gender		
Male	260	61
Female	216	59
Prior diagnoses		
Malignancy (various locations n=20; lung n=8)	28	74
Pneumonia	32	50
COPD/asthma/chronic bronchitis	90	63
History taking		
Smoking	93	66
Haemoptysis	32	60
Cough	264	67*
Dyspnoea	129	65
Fever	36	68
Abnormalities during physical examination†	219	69*
Suspected diagnosis pneumonia according to GP	132	68*
Suspected diagnosis malignancy according to GP	91	64

* $p \leq 0.05$

† A physical examination was considered abnormal when abnormalities were detected with auscultation (e.g. wheeze), percussion (e.g. dullness), or palpation (e.g. pain)

therapy (from 24% to 15%), especially fewer prescriptions of drugs such as antibiotics; and more frequent reassurance of the patient (from 25% to 46%).

To our knowledge this is the first study that has investigated the influence of CXR on patient management in general practice. The studies of Guyer et al[9] and Keogan et al[10] reported numbers of clinically relevant abnormalities in 21% and 23%, respectively, of patients referred for CXR by GPs. The 24% clinically relevant abnormalities found in our study is comparable. In addition, our study showed that the full value of CXR cannot be assessed in terms of positive findings alone. Negative findings are important for exclusion of diseases and, therefore, for reassurance of the patient. However, such findings can also result either in referral of patients to a medical specialist for further evaluation of their complaints when a CXR fails to show any abnormalities, or in the referral of patients to another medical specialist, such as a cardiologist, when lung pathology is excluded.

Subgroup analyses revealed that the proportion of patients in whom patient management changed after CXR was significantly higher among patients with complaints of cough (67%), exhibited abnormalities during physical examination (69%) or a suspected diagnosis of pneumonia (68%). The changes in GPs' patient management plans after CXR in these patients were fewer anticipated referrals to a medical specialist, a reduction in the number of patients with initiation or change in therapy and more frequent reassurance of the patient. It is widely known that thorough history taking and physical examination before commencement of a more advanced workup, such as a radiological examination, is very important. This study showed that even after a history and physical examination of the patient the influence of CXR on patient management was substantial. We expected that the ability of GPs to establish a more specific patient management plan after gaining detailed information of the patient with physical examination would result in a smaller proportion change in management after CXR. However the proportion of change in patient management increased to almost 70% in patients with abnormalities detected during physical examination.

Almost 80% of the questionnaires were returned by the patients, which increased the validity of these results. Approximately 50% of patients were reassured by their GP after CXR. Our study showed that in almost one-quarter of the patients who were reassured by their GP after CXR, the patient did not perceive this as reassurance. Therefore, CXR did not have much value for these patients, because no referral or treatment followed after the radiological investigation and reassurance was not achieved.

Before we can reach a conclusion it is important to note that this study has several limitations. It was impossible to verify whether or not the GP really would have conducted the anticipated patient management in accordance with the plan made on the standardized form before CXR was performed. This could result in an overestimation of intended referrals to medical specialists. This study does not prove that the patient actually benefits from the diagnostic procedure, e.g. in terms of morbidity, mortality or quality of life. However, the study is the first to show that the procedure often leads to changes in patient management, which is one of the prerequisites for successfully influencing clinically relevant patient outcomes.

In conclusion, the GP's patient management strategy was changed for 60% of patients following CXR. CXR substantially reduced the number of referrals to a medical specialist and initiation or change in therapy, and more patients were reassured by their GP. Thus, CXR is an important diagnostic tool for GPs and seems to reduce the burden on patients and health care.

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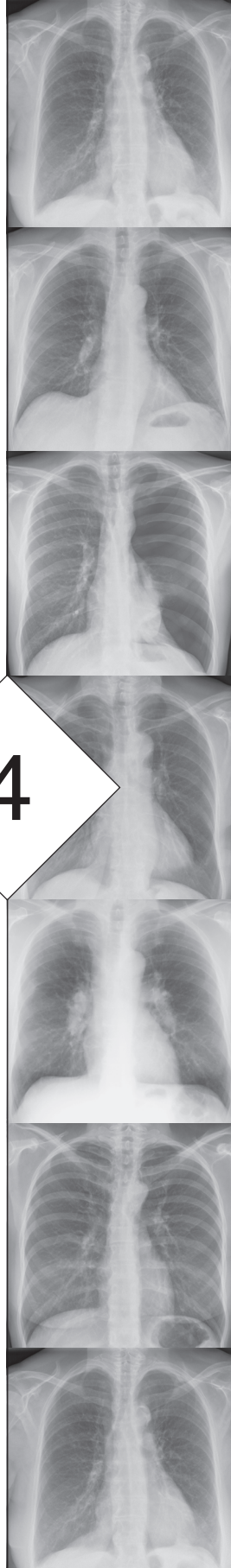
Chest radiography in patients suspected of pneumonia in primary care: diagnostic yield, and consequences for patient management



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Speets AM, Hoes AW, Van der Graaf Y, Kalmijn S, Sachs APE, Mali WPThM. Chest radiography in patients suspected of pneumonia in primary care: diagnostic yield, and consequences for patient management. In revision for Eur Respir J.

Abstract

Background. Chest radiography (CXR) is frequently performed for diagnosing pneumonia in primary care. This prospective cohort study assessed the diagnostic yield of CXR in primary care patients suspected of pneumonia.

Methods. In total, 192 patients with a clinical suspicion of pneumonia aged ≥ 18 years (mean age 56.8±17.6 years; 55% males) were referred by their general practitioner (GP) for CXR to one of the three participating hospitals in The Netherlands. All GPs were asked to fill in a standardized form before and after CXR. The primary outcome measures were the proportion of patients with a clear shift in the probability estimation of pneumonia, and the proportion patients with a change in patient management following CXR.

Results. Pneumonia was diagnosed by GPs in 35 patients (18%), of whom 27 patients (14%) had a positive CXR, and 8 patients (4%) a negative CXR, however with an assumed high probability of pneumonia by the GP. CXR clearly influenced the diagnosis of pneumonia by the GP in 53% of the patients: CXR ruled out pneumonia in 47%, and the probability of pneumonia substantially increased in 6% of the patients. Patient management changed after CXR in 69% of the patients, mainly caused by a reduction in medication prescription (from 43% to 17%); and more frequent reassurance of the patient (from 8% to 35%).

Conclusion. CXR is an important diagnostic tool in primary care patients with a clinical suspicion of pneumonia in terms of change in the estimated probability of pneumonia, and change in patient management.

Introduction

Primary care physicians usually rely on patient history, and signs and symptoms to diagnose or exclude pneumonia.[1] However, most signs and symptoms traditionally associated with pneumonia (e.g. fever and coughing) are not predictive of pneumonia in general practice.[2-4] Chest radiography (CXR) is the most frequently performed diagnostic investigation requested by general practitioners (GPs) in Europe: in 22% of patients with a suspected lower respiratory tract infection CXR is requested.[5] CXR is considered the gold standard for pneumonia diagnosis. CXR can diagnose pneumonia in case of presence of an infiltrate, and differentiate pneumonia from other conditions that may present with similar symptoms (e.g. acute bronchitis). In addition, the results may suggest specific aetiologies (e.g. lung abscess), identify coexisting conditions (e.g. bronchial obstruction), and evaluate the severity of illness.[6-9]

Although CXR is frequently used for diagnosing pneumonia, little is known about the influence of CXR on the probability estimation of pneumonia by GPs, and on change in patient management. Simpson et al concluded that results of CXR requested by GPs influenced patient management in 48% of 97 patients with radiographic features of acute infection.[10] However, this study was conducted only in patients with radiographic evidence of infection and the patient management was assessed with questionnaires filled in retrospectively by GPs. When assessing the diagnostic yield of CXR, e.g. in terms of patient management, it is important to study the complete cohort of patients suspected of pneumonia, and not only the subgroup of patients with a radiographic diagnosis of pneumonia.

The objective of this prospective cohort study was to assess the effect of CXR on the probability estimation of pneumonia by GPs, the influence of CXR on patient management and consequences of CXR according to the patient. The study population consisted of primary care patients with a clinical suspicion of pneumonia referred for CXR by GPs.

Methods

This study is part of a large prospective cohort study conducted from April 2003 to December 2004 with the help of 78 GPs participating in the catchment area of one of three general hospitals located in three main cities in The Netherlands (Jeroen Bosch Hospital in 's-Hertogenbosch; Gelre Hospitals in Apeldoorn; 'Onze Lieve Vrouwe Gasthuis' in Amsterdam). In total 870 patients of 18 years and older who

were referred for CXR (posteroanterior and lateral view) by their GP to one of these hospitals were included in the cohort study. The study was approved by the Medical Ethics Review Board.

The GPs could fill in three probable diagnoses on a standard form before requesting a CXR. In the present study all patients who were referred for CXR with a clinical suspicion of pneumonia as one of these probable diagnoses were included (n=222). Estimated probabilities for 18 patients (8%) were not filled in by the GP before and/or after CXR. These patients were excluded from the study. Their patient characteristics were comparable with the included patients. Patients referred for a follow-up CXR for the treatment evaluation of pneumonia were also excluded (n=12), resulting in a study population of 192 patients. Additionally, all patients with incidental pneumonia detected with CXR were included as a separate patient group (i.e. patients referred for CXR without a clinical suspicion of pneumonia).

All GPs were asked to fill in a standardized form before requesting a CXR, including information on history, physical examination, indication, probable diagnosis with estimated prior probabilities on a visual analogue scale (range 0-100%), and anticipated patient management. The management options included: referral to a medical specialist; medication prescription; reassurance of the patient; and follow-up by the GP (watchful waiting or additional diagnostic testing). After the GP received the report (within 1-4 days after the CXR) he or she filled in a second questionnaire, again including the probable diagnosis with estimated posterior probabilities, and anticipated patient management plan. We considered a decrease or increase in the estimated probability of pneumonia by the GPs after CXR of ≥ 30% as a substantial change in the probability estimation.

The findings on the CXR were categorized into four groups: (1) pneumonia; (2) other clinically relevant abnormalities; (3) a known abnormality, which was detected previously on CXR; (4) no abnormality. Six months after the CXR a short questionnaire was sent to all patients (response rate 84%), in order to evaluate their current complaints and assess the consequences of CXR according to the patient.

The primary outcome measures for our study were the proportion of patients with a clear shift in the probability estimation of pneumonia by the GP (≥ 30% decrease or ≥ 30% increase of the estimated probability after CXR), and the proportion of patients in whom there was a change in patient management by the GP following CXR. These proportions and corresponding 95% confidence intervals were calculated using the statistical program Confidence Interval Analysis.[11]

TABLE 1. Patient characteristics (n=192)

	n (%)
Age (mean ± sd in years)	56.8±17.6
Gender (male)	106 (55)
Prior diagnoses	
Malignancy (various locations n=7; lung n=2)	9 (5)
Pneumonia	28 (15)
COPD/asthma/chronic bronchitis	48 (25)
Recent prescription of antibiotics	45 (23)
History taking	
Smoking	32 (17)
Pain	27 (14)
Haemoptysis	13 (7)
Cough	127 (66)
Dyspnoea	54 (28)
Other symptoms of respiratory infection*	39 (20)
Fever	33 (17)
General malaise	25 (13)
Physical examination	
Abnormalities during auscultation	113 (59)
Abnormalities during percussion	49 (26)

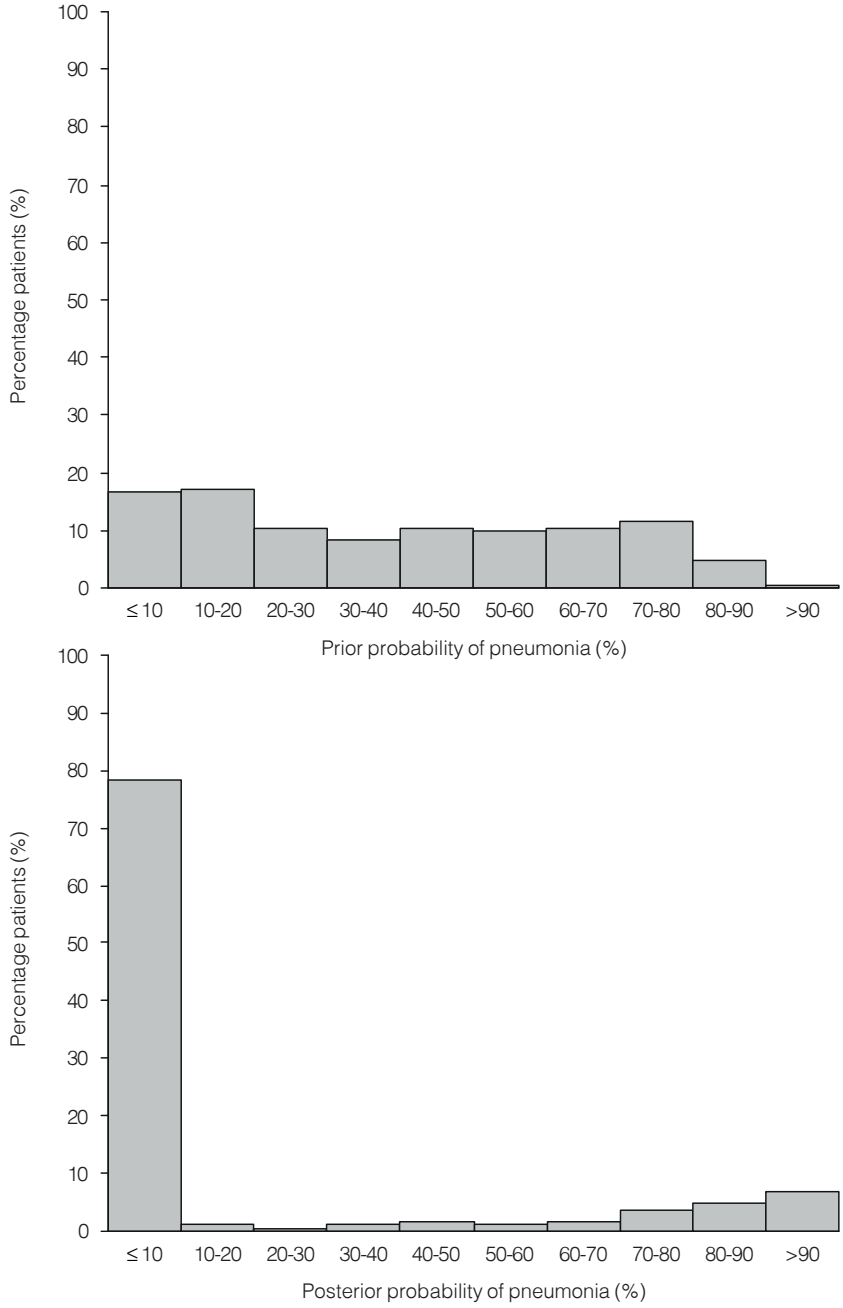
* Abnormal sputum, nasal congestion, throat symptoms, and complaints of a cold

Results

The mean age of the patients with a clinical suspicion of pneumonia was 56.8±17.6 years, and 55% were male. Fifteen percent of the patients had a prior diagnosis of pneumonia. Cough was the most frequently reported symptom among the patients (66%). Abnormalities during auscultation and percussion were found in respectively 59% and 26% of the patients (Table 1).

The radiology reports of CXR showed pneumonia in 27 patients (14%); other clinically relevant abnormalities in 32 patients (17%); a known abnormality, which was detected previously on CXR in 35 patients (19%) and no abnormality in 98 patients (52%). The group other clinically relevant abnormalities consisted of 1 malignancy, 23 patients with COPD/asthma/chronic bronchitis, 4 abnormalities that required further investigation, and 4 other abnormalities (e.g. diaphragmatic hernia).

FIGURE 1. Distribution of the probabilities of pneumonia estimated by the general practitioners before and after chest radiography



The distributions of the prior and posterior probability of pneumonia are shown in Figure 1. Noticeable were the two large groups referred for CXR with a very low or high prior probability of pneumonia, 64 patients (33%) and 30 patients (16%) respectively. After CXR, pneumonia was diagnosed in 4 of the 64 patients (6%) with a very low prior probability, and in only 15 of the 30 patients (50%) with a very high prior probability of pneumonia. The probability estimation of pneumonia was clearly changed by means of CXR in 53% of the patients (95% CI 46%-59%). The estimated probability of pneumonia decreased with ≥ 30% (range 30-100%) in 89 patients (47%), and increased with ≥ 30% (range 30-80%) in 12 patients (6%) after CXR.

The proportion of patients for whom patient management changed following CXR was 69% (95% CI 62%-75%). Main changes in patient management plans after CXR included: a reduction in the number of patients with a medication prescription from 79 (43%) to 32 (17%) patients; and more frequent reassurance of the patient, from 15 (8%) to 64 (35%) patients (Table 2). The reduction in medication prescription was caused mainly by a decrease in the prescription of antibiotics from 53 patients (28%) before CXR to 26 patients (14%) after CXR.

Six months after the CXR the current complaints were diminished or disappeared in almost 80% of the patients referred for CXR by GPs with a clinical suspicion of pneumonia. Only 15% of the patients who returned the questionnaire reported that CXR had no value for him or her. CXR resulted in a definite diagnosis or better treatment according to 43% of the patients, and 44% of the patients were reassured after CXR.

Pneumonia was diagnosed with CXR in 27 patients (14%), with a mean age of 53.8±18.8 years, and 44% were male. Abnormalities during auscultation and percussion were found in respectively 74% and 26% of these patients. The GPs referred 7 patients (26%) to a medical specialist, medications were prescribed in 13 patients (48%), patient management was watchful waiting in 6 patients (22%), and an additional CT scan was ordered for 1 patient (4%). Six months after the CXR the current complaints were diminished or disappeared in 72% of the patients, and 8% reported that CXR had no value for him/her.

Additionally, pneumonia was diagnosed by the GP in 8 patients (4%) without a positive CXR, however with an assumed high probability of pneumonia by the GP. The GP suspected pneumonia in 4 patients, viral pneumonia in 2 patients, and mycoplasma pneumonia was shown with additional laboratory investigation in 2 patients. The 4 patients suspected of pneumonia were: 1) 48-years old male with a medical history of COPD, 2 weeks complaints of cough and thoracic pain, without abnormalities during physical examination; 2) 52-years old female who smoked,

TABLE 2. Patient management plans of general practitioners before and after chest radiography*

BEFORE(n) / AFTER (n (%))	Referral medical specialist	Medication prescription	Reassurance	Follow-up by GP†	Total
Referral medical specialist	**10 (24)**	14 (18)	1 (7)	4 (8)	29 (16)
Medication prescription	7 (17)	**19 (24)**	0	6 (12)	32‡ (17)
Reassurance	16 (38)	18 (23)	**10 (67)**	20 (41)	64‡ (35)
Follow-up by GP†	9 (21)	28 (35)	4 (27)	**19 (39)**	60 (32)
Total	42 (23)	79 (43)	15 (8)	49 (26)	185

* Patient management plans for 7 patients (4%) were not filled in by the GP before and/or after chest radiography

† Follow-up by GP: predominantly watchful waiting or additional diagnostic testing, such as spirometry or laboratory investigation

‡ The differences in proportions of patient management after chest radiography were significant with a p-value ≤ 0.05

1 week complaints of cough, dyspnoea and fever, without abnormalities during physical examination; 3) 62-years old female with a colleague diagnosed with pneumonia, 1.5 week complaints of cough, and crepitations on the left side; 4) 20-years old female with an infiltrate in her medical history (2.5 years ago), some days complaints of cough, thoracic pain and fever, and without abnormalities during physical examination. After CXR 4 of the 8 patients were referred to a medical specialist, and medications were prescribed in 4 patients. Six months after the CXR the current complaints were diminished or disappeared in 71% of the patients, and 14% reported that CXR had no value for him/her.

Small infiltrates or early manifestations of pneumonia were found as an incidental finding with CXR in 5 patients (age range 32-77 years; 3 males) of the total cohort of 870 patients (<1%). Two patients were referred for CXR for the exclusion of a

malignancy, 1 patient for the confirmation of COPD, and 2 patients had unclear complaints without any abnormalities during physical examination. After CXR 3 patients were referred to a medical specialist, medications were prescribed in 1 patient, and patient management was watchful waiting and an additional follow-up CXR in 1 patient.

Discussion

CXR clearly influenced the diagnosis of pneumonia by the GP in 56% of the patients referred for CXR with a clinical suspicion of pneumonia: CXR ruled out pneumonia in 50% of the patients, and the probability of the diagnosis pneumonia substantially increased in 6% of the patients. The proportion of patients for whom patient management changed following CXR was 69%, mainly caused by a decrease in the prescription of antibiotics, and more frequent reassurance of the patient.

To our knowledge, this study is the first that assessed the effect of CXR on the probability estimation of pneumonia by GPs. The number of patients in whom the patient management changed (69%) is much higher than the 48% reported in the study of Simpson et al.[10] This difference could be explained by the study designs: their study was conducted in patients with radiographic evidence of infection and the patient management was assessed with questionnaires filled in retrospectively by GPs, which may have biased the results. Besides, Simpson et al did not specify whether reassurance of the patient was considered as patient management, and how patient management was influenced by the findings of CXR.

The distributions of the prior and posterior probability of pneumonia in Figure 1 showed that the uncertain area of a diagnosis, around estimated probabilities of 50%, disappeared largely as a consequence of CXR. Noticeable in our study was that almost half of all patients were referred for CXR with a very low or high prior probability of pneumonia, respectively 33% and 16% of the patients. Seventy-five percent of the patients with a very low prior probability of pneumonia had additional differential diagnoses, such as COPD or acute bronchitis, with a higher prior probability according to the GP. After CXR, pneumonia was diagnosed in 6% of the patients with a very low prior probability, and in only 50% of the patients with a very high prior probability of pneumonia. This emphasizes the importance of referring patients with a clinical suspicion of pneumonia for CXR, even when the prior probability of pneumonia is very high according to the GP.

Pneumonia was diagnosed by the GP in 35 patients (18%): 27 (14%) had a positive CXR, and 8 patients (4%) a negative CXR, however with an assumed high probability of pneumonia by the GP. Low percentages of patients diagnosed with

pneumonia by a positive CXR were also found in other studies: 15% by Melbye et al[12], and 7% by Lieberman et al.[13] It is noticeable that the estimated probabilities in the patient groups diagnosed with pneumonia with a positive and negative CXR were high before CXR, 61% and 72% respectively. However, these percentages were not high enough for the GPs to start treatment or refer patient to a medical specialist without an additional CXR. The current restrictive policy of prescribing antibiotics could encourage the GPs to order CXR in patients suspected of pneumonia even when estimated prior probabilities are high based on medical history, anamnesis and physical examination.[9]

The manifestations of pneumonia on CXR may vary considerably, depending upon the degree of inflammation and the stage of the disease process. It is difficult to diagnose mild or early stage pneumonia by CXR.[14,15] Besides, it is possible to detect pneumonia during physical examination without roentgengraphic evidence.[14] The 8 patients with a high estimated probability of pneumonia, and a negative CXR might have been referred too soon for CXR by their GP; mycoplasma pneumonia was shown with additional laboratory investigation in 2 of these 8 patients.

Interestingly, no clear differences in patient characteristics, including signs and symptoms, were observed in referred patients with or without pneumonia. This indicates that the GPs adequately applied their clinical skills to select those patients for additional imaging in whom history taking and physical examination provided insufficient information to distinguish those with from those without pneumonia.

As expected, pneumonia was found scarcely as incidental finding with CXR. In our study, small infiltrates or early manifestations of pneumonia were found as an incidental finding in less than 1% of the patients of the total cohort of 870 patients.

A limitation of our study is that it was impossible to verify whether or not the GP really would have conducted the anticipated patient management in accordance with the plan made on the standardized form before CXR was performed. This could result in an overestimation of intended referrals to medical specialists.

In conclusion, CXR is a valuable diagnostic tool in primary care patients with a clinical suspicion of pneumonia referred for CXR by GPs in terms of change in the estimated probability of pneumonia by GPs, change in patient management, and according to the patients themselves. In particular, CXR is important for the exclusion of pneumonia in general practice.

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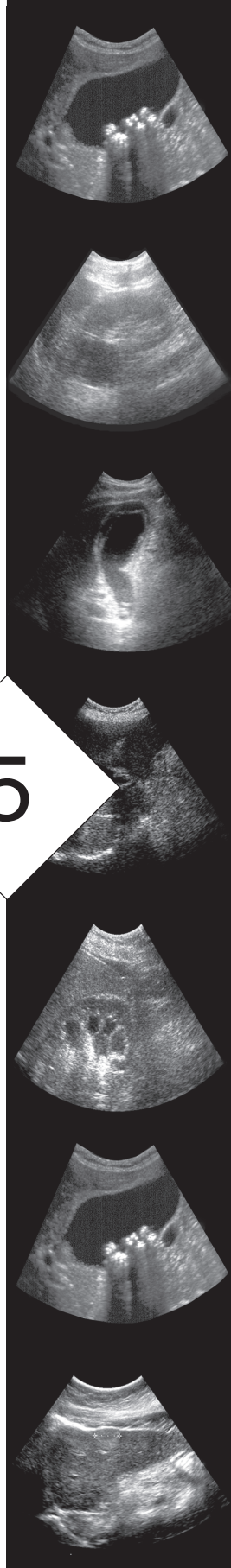
The value of abdominal ultrasound in patients with abdominal pain referred by general practitioners



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Speets AM, Kalmijn S, Hoes AW, Van der Graaf Y, Mali WPThM. The yield of abdominal ultrasound in patients with abdominal pain referred by general practitioners. Submitted.

Abstract

Background. About 8% of the patients with abdominal pain of unclear origin are referred by general practitioners (GPs) for abdominal ultrasound (US). The objective of this study was to examine the prevalence and determinants of significant abnormalities on abdominal US in patients with abdominal pain referred by GPs.

Methods. This cross-sectional study was conducted with data from the computerized hospital database of University Medical Centre Utrecht in The Netherlands from January to December 2002, if necessary completed with data from an additional patient questionnaire. Findings on US were considered as significant abnormalities when it resulted in referral to a medical specialist or hospital admission.

Results. In total, 499 patients of 18 years and older with abdominal pain were referred for abdominal US by GPs. Mean age at time of the US was 47.9 years (sd 15.2), and almost one third was male. Significant pathology was seen in 16% of the patients. Older age (OR 1.03 per year), colicky pain (OR 2.80) and a clinical suspicion of bile stones (OR 2.31) were predictors of a significant abnormal finding on abdominal US.

Conclusion. A significant abnormality was found in 16% of the patients aged 18 years and older with abdominal pain, who were referred for abdominal US by GPs. Older age, colicky pain, and a clinical suspicion of bile stones were predictors of a significant abnormal finding on abdominal US.

Introduction

Many problems encountered by general practitioners (GPs) are of a non-acute, non-specific nature, such as abdominal complaints.[1] Approximately half of all abdominal complaints consist of pain.[2] The two-year cumulative incidence of abdominal pain in The Netherlands is estimated at 3%.[3] Patients with abdominal pain comprise 2% to 4% of all visits to GPs.[4-6] Results of three previous studies are consistent with the impression that abdominal pain in general practice usually is a self-limiting disease for which no definitive diagnosis is found and which can be managed entirely by the GP.[5-7]

One of the most difficult tasks confronting the GP is knowing how extensive a particular symptom has to be investigated, taking into account that performing unnecessary radiological investigations can lead to incidental findings, extra costs and be a burden for the patient. On the other hand, investigations with negative findings may also be of importance in daily practice, for purposes of reassurance. In the case of abdominal pain, this dilemma is stressed by the availability of a wide range of sophisticated diagnostic technology.[8] In this range, ultrasound (US) is the least expensive and most non-invasive abdominal imaging modality and a safe and effective diagnostic procedure.[9-11]

Abdominal pain is one of the indications for the performance of an US examination of the abdomen in the American College of Radiology standards.[12] About 8% of the patients with abdominal pain of unclear origin are referred by GPs for abdominal US. [6,10] Annually, about 200,000 abdominal US are on request of GPs in The Netherlands. It is unclear whether, and in which patients abdominal US yields sufficiently relevant information. Abdominal US among patients with abdominal pain has received little attention in the scientific literature. The purpose of this cross-sectional study was to examine the prevalence and determinants of significant abnormalities on abdominal US in patients with abdominal pain referred by GPs.

Methods

The study sample was taken from the Hospital Information System computer database of the University Medical Centre (UMC) Utrecht in The Netherlands. A cross-sectional study was conducted, covering the period from January to December 2002. All patients referred by their GPs for abdominal US were extracted from the database, in which all data of the US referral forms filled in by the GPs and US findings were available. Patients of 18 years and older were included when

complaints of abdominal pain or a clinical suspicion of bile and/or renal stones by the GP were indicated at the referral form of the GP. A total of 911 abdominal US were performed for GPs in UMC Utrecht during this period, and 499 (55%) patients met the inclusion criteria. In The Netherlands no approval by the Medical Ethics Review Board and no informed consent is required when a medical specialist, in this case the radiologist, evaluates his own patient management.

Gender, age, indications and information about the findings were collected from the patient files in the computer database. The indications were arranged in four groups: complaints of pain, other symptoms than pain (e.g. nausea), relevant medical history (e.g. previous surgery), and a clinical suspicion of the GP (e.g. presence of bile stones).

Abdominal US can result in multiple findings. These findings were initially categorized in four groups: no abnormality, non-relevant abnormality (steatotic liver, fatty pancreas, and other findings e.g. obstipation, simple cysts and retroflection uterus), abnormality with unclear consequences (bile stones, benign solid tumour, renal problems, renal stones, hernia inguinalis, and pathology aorta abdominalis) and significant abnormality (malignant tumour, pathology gallbladder, and perforation liver). A short questionnaire was sent to 146 patients with an abnormality with unclear consequences, in order to assess the consequences of the US finding. In total, 115 (79%) questionnaires were returned. The remaining 21% of the patients were checked in the Hospital Information System and at the general practices, resulting in complete follow-up. Findings of US were considered to be a significant abnormality when it resulted in referral to a medical specialist or hospital admission. In the logistic regression analysis the most serious finding of each patient was used as the outcome.

Multivariate logistic regression analysis was used to investigate whether gender, age, complaints of pain, other symptoms than pain, medical history and a clinical suspicion of the GP were independent determinants of a significant abnormal finding on abdominal US. Statistical significance was inferred when the p-value was equal to or less than 0.05. Data were analysed using SPSS for Windows version 11.0.

Results

Mean age at time of the abdominal US was 47.9 years (sd 15.2), and almost one third was male (30%). Table 1 gives an overview of indications for abdominal US. A large part of the patients had complaints of localized abdominal pain (51%) or abdominal pain e causa ignota (eci) (30%). In 10% colicky pain was the indication

TABLE 1. Patient characteristics (n=499)

	n (%)
Age (mean ± sd in years)	47.9±15.2
Gender (male)	150 (30)
Complaints of pain	
Abdominal pain eci	149 (30)
Localized abdominal pain	252 (51)
Colicky pain	50 (10)
Other symptoms	
Nausea/vomiting	24 (5)
Liver function disorder	16 (3)
Relevant medical history	94 (19)
Clinical suspicion of the GP	
Bile stones	125 (25)
Renal stones	32 (6)
Other clinical suspicion	91 (18)

for abdominal US. In roughly half of the cases, clinical suspicions were mentioned, with a specific clinical suspicion of presence of bile stones in 25% and renal stones in 6%.

Significant abnormalities were detected with abdominal US in 81 patients (16%), a non-relevant abnormality in 214 (43%), and no abnormality in 204 patients (41%). Bile stones were detected often with abdominal US, in 72 of 499 patients (14%). Forty-four of these 72 bile stones (61%) were significant abnormalities and eventually resulted in laparoscopic cholecystectomy in 40 patients (56%).

Figures 1A to 1C illustrate the associations of age, abdominal complaints and clinical suspicions with the finding categories of abdominal US. Figure 1A shows an increase of non-relevant and significant abnormalities with age, while a marked decrease of the category no abnormality is seen. The discontinuation of the increase of significant abnormalities after the age of 58 years is remarkable. Figure 1B shows that complaints of abdominal pain eci or localized abdominal pain resulted in larger percentages of the category no abnormality. Significant abnormalities occurred most often when complaints of colicky pain were present. Also a clinical suspicion of bile stones often resulted in a significant abnormality on US (Figure 1 C). When no specific clinical suspicion was mentioned in the indication, relatively more US showed no abnormality in comparison to the presence of a clinical suspicion in the patient files.

FIGURE 1A. Findings on abdominal ultrasound by age group

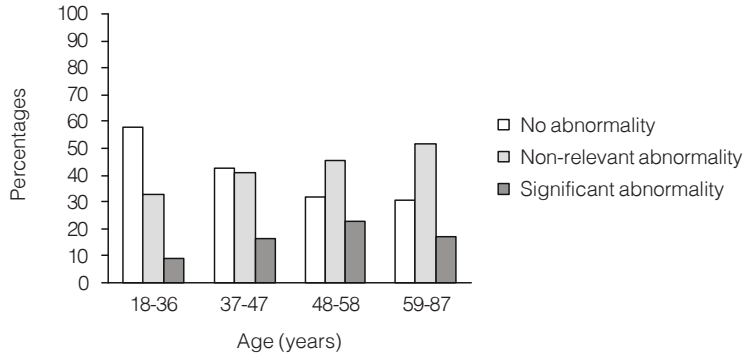

FIGURE 1B. Findings on abdominal ultrasound by complaints of abdominal pain

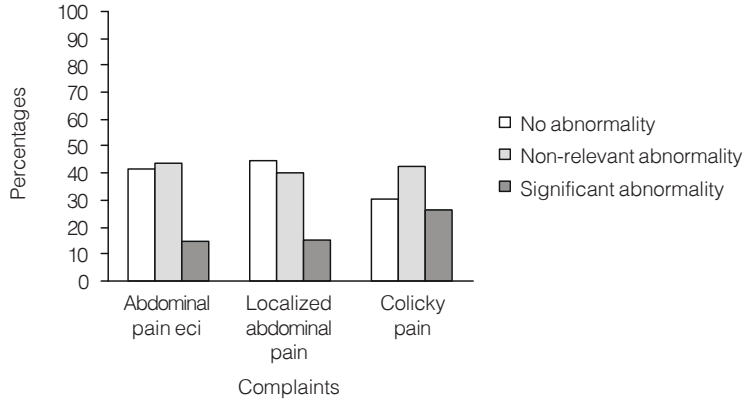

FIGURE 1C. Findings on abdominal ultrasound by clinical suspicion

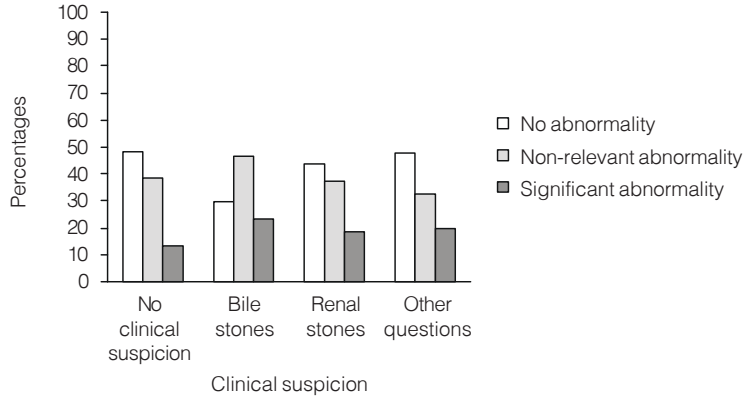

TABLE 2. The relation of baseline characteristics and indications with significant abnormality on abdominal ultrasound in 499 patients by multivariate logistic regression analysis

	Significant abnormality n (%)	Odds ratio	95% confidence interval
Gender			
Female	52 (15)	ref.	ref.
Male	29 (19)	1.43	0.84-2.43
Age (each year)	-	1.03*	1.01-1.04
Complaints of pain			
Abdominal pain eci	36 (14)	1.18	0.45-3.08
Localized abdominal pain	22 (15)	1.19	0.48-2.97
Colicky pain	14 (28)	2.80*	1.02-7.66
Other symptoms			
Nausea/vomiting	7 (29)	2.09	0.80-5.45
Liver function disorder	1 (6)	0.34	0.04-2.67
Relevant medical history	15 (16)	1.13	0.59-2.15
Clinical suspicion of the GP			
Bile stones	30 (24)	2.31*	1.22-4.40
Renal stones	6 (19)	1.36	0.48-3.87
Other clinical suspicion	13 (14)	1.15	0.57-2.34

* $p \leq 0.05$

Multivariate logistic regression analysis identified three relevant determinants of significant abnormal findings on abdominal US (Table 2). Aging was associated with an increased risk of a significant abnormality of 3% per year (95% CI 1.01-1.04). Colicky pain and a specific clinical suspicion of the presence of bile stones increased the risk of an abnormal finding more than twofold, with a 95% CI of respectively 1.04-7.66 and 1.26-4.40.

Discussion

This cross-sectional study provides insight into the indications for and findings of US in patients with abdominal pain referred by GPs. Significant abnormalities were seen in 16% of all abdominal US. Older age, colicky pain, and a clinical suspicion of bile stones were predictors of a significant abnormal finding on abdominal US.

Abdominal US among patients with abdominal pain referred by GPs has received little attention in the scientific literature. We found only four studies on abdominal US requested by GPs, but these were not specifically performed in patients with

abdominal pain.[13-16] None of these studies formulated clear definitions of significant abnormalities or examined the indications in relation to findings on abdominal US. Significant abnormalities were detected on 25% to 30% of the abdominal US.[13-16] Only Charlesworth et al[14] presented percentages for relevant abnormalities in patients with left upper quadrant pain (n=27) and patients referred with lower abdominal pain (n=100): 18% for both patient groups. This percentage is comparable with the 16% significant abnormalities found in our study.

The present study showed three determinants of significant abnormal findings on abdominal US, i.e. age, colicky pain and a clinical suspicion of bile stones. It is well known that morbidity increases with age. Our finding of a significant positive association of age with abnormal findings on abdominal US agrees with the study of Muris et al[17], that also showed a positive association between age and organic disease in patients with abdominal pain. The discontinuation of the increase in the number of significant abnormalities after the age of 58 years was remarkable. It is possible that for example bile stones are more often found as incidental findings during the search for severe pathology; or GPs referred relatively older patients with only few alarming complaints for abdominal US, leading to relatively few severe abnormalities. As expected, a significant association was found between colicky pain and significant abnormalities on abdominal US. A similar association was observed for a clinical suspicion of bile stones. The presence of a clinical suspicion of renal stones and other suspicions also showed a positive, but non-significant association. These associations are in line with the statement by Muris et al[6] that thorough initial history and physical examination in abdominal pain patients before commencing a more advanced workup is very important.

Certain limitations of the study should be discussed. First, we used an existing data file for collection of information about indications and findings on abdominal US, which can lead to incomplete data and some distortion of the results. Secondly, the study was conducted in a university hospital. In The Netherlands, GPs can choose to refer patients to a regional or university hospital. Patients suspected of more serious illnesses or who have been in the university hospital for other reasons than abdominal pain may have a larger chance of being referred to this hospital. The prevalence of pathologic findings of 16% could therefore be an overestimation, although Charlesworth et al[14] presented percentages of 18% relevant abnormalities in patients with abdominal pain and the other percentages mentioned previously ranged from 25 to 30%.

Several questions are raised by the results of this cross-sectional study: What is the value of abdominal US in the 84% of the patients in whom no or non-relevant abnormalities were found? Do results of abdominal US change patient management decisions of GPs or have an effect on the outcome of illness? Can specific patient subpopulations be indicated, in whom abdominal US is of additional value? To gain more insight into the additional value of abdominal US in general practice we are planning to perform a prospective study in multiple general practices and hospitals.

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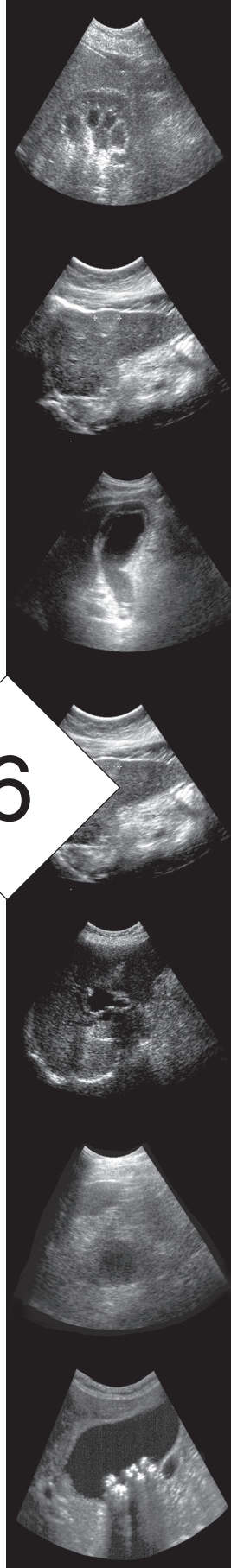
Indications and consequences of upper abdominal ultrasound in general practice



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Speets AM, Hoes AW, Van der Graaf Y, Kalmijn S, De Wit NJ, Montauban van Swijndregt AD, Gratama JWC, Rutten MJCM, Mali WPThM. Upper abdominal ultrasound in general practice: indications, diagnostic yield, and consequences for patient management. In revision for Fam Pract.

Abstract

Background. Abdominal ultrasound (US) is frequently performed in Western societies. There is insufficient knowledge of its diagnostic value in terms of changes in patient management decisions in primary care. The objective of this study was to assess the influence of upper abdominal US on patient management in general practice.

Methods. A prospective cohort study with 76 general practitioners (GPs) and three general hospitals in The Netherlands. 395 patients aged ≥ 18 years referred by their GPs for upper abdominal US were included. The main outcome was change in anticipated patient management assessed by means of questionnaires filled in by GPs before and after abdominal US.

Results. Mean age of the patients was 54.0±15.8 years, 35% were male. Clinically relevant abnormalities were found in 29% of the abdominal US, mainly cholelithiasis. Anticipated patient management changed in 64% of the patients following abdominal US. Main changes included: fewer referrals to a medical specialist (from 45% to 30%); and more frequent reassurance of the patient (from 15% to 43%). However, this reassurance was not perceived as such in almost 40% of these patients. A change in anticipated patient management occurred significantly more frequently in patients with a prior cholecystectomy (82%).

Conclusion. Anticipated patient management by the GP changed in 64% of patients following upper abdominal US. Abdominal US substantially reduced the number of intended referrals to a medical specialist, and more patients could be reassured by their GP.

Introduction

Abdominal ultrasound (US) is an important diagnostic method for evaluation of many structures in the abdomen, such as the liver, gallbladder, biliary tract, pancreas and kidneys. Indications include abdominal, flank and/or back pain, palpable abnormalities, abnormal laboratory values suggestive for abdominal pathology, follow-up of known or suspected abnormalities and search for metastatic disease or occult primary.[1] Abdominal US is frequently performed in Western societies. Annually, about 200,000 abdominal ultrasounds are requested by GPs in The Netherlands, usually performed in referral hospitals.

The frequency with which even relatively inexpensive and non-invasive diagnostic tests are performed clearly places a burden on health care. Therefore it is important that their influence on patient management is assessed. Unnecessary diagnostic investigations may lead to incidental findings, or to additional unnecessary diagnostic procedures or even over treatment.

Evaluations of abdominal US in patients referred by GPs have scarcely been reported in the scientific literature. There is insufficient knowledge of its diagnostic value in terms of changes in patient management decisions in primary care. We are aware of four retrospective studies that examined abdominal complaints and referral by GPs for abdominal US.[2-5] The percentages of clinically relevant abnormalities detected on abdominal US ranged from 25% to 30%. Clearly, the full value of abdominal US cannot be assessed in terms of positive findings alone. Firstly, the relevance of detected abnormalities must be assessed with respect to clinical practice, because positive findings may be incidental and without any consequences. Positive findings are relevant only when they result in changes of patient management. On the other hand, negative examinations can also have potential value when they result in changes of patient management and can be very helpful in reassuring patients. Neither of these studies however cited both positive and negative findings in detail, nor assessed the value of abdominal US in terms of changes in patient management. Also, the consequences of abdominal US according to the patient were not studied before.

The objective of this study was to assess the influence of both positive and negative findings of upper abdominal US on the change in patient management in general practice and to evaluate the consequences of the abdominal US according to the patient.

Methods

This prospective cohort study was conducted from April 2003 to December 2004. In total, 76 GPs in the catchment area of one of three participating general hospitals located in three main cities in The Netherlands (Jeroen Bosch hospital in 's-Hertogenbosch; Gelre hospitals in Apeldoorn; 'Onze Lieve Vrouwe Gasthuis' in Amsterdam) were involved. 25 GPs (33%) worked in a solo practice, 54 (71%) were male, 32 GPs (42%) graduated between 1968-1980, 23 (30%) between 1980-1990, and 21 (28%) between 1990-1997. All patients of 18 years and older who were referred for upper abdominal US by their GP to one of these hospitals were included in the study. The patients received an exclusion form from their GP, which they could return to the study coordinator if we were not allowed to use their data for this study. This study was approved by the Medical Ethics Review Board.

All GPs were asked to fill in a standardized form before requesting an upper abdominal US, including information on history, physical examination, indication, suspected diagnosis, and proposed patient management. The anticipated patient management was filled in as if no abdominal US would be performed. The management options included: referral to a medical specialist; initiation or change in therapy; follow-up by the GP (watchful waiting or additional diagnostic testing); and reassurance of the patient. The GP could choose only one of these management options. After the GP received the report (within 1-4 days after the US) he or she filled in a second questionnaire; again including the suspected diagnosis and anticipated patient management plan.

The reports of upper abdominal US were collected in the three hospitals to determine the findings of the US. These findings were categorized into six groups: (1) malignancy; (2) cholelithiasis; (3) nephrolithiasis; (4) other significant abnormalities (e.g. abdominal aortic aneurysm and unclear abnormalities that required further investigation according to the radiologist); (5) follow-up of abnormalities detected previously on abdominal US; (6) no abnormality. The first four groups were considered clinically relevant abnormalities.

Six months after the abdominal US a short questionnaire was sent to all patients, in order to assess the value and consequences of abdominal US according to the patient (response rate 81%). They could choose one of the following options: definite diagnosis; better treatment; reassurance; nothing; or other. With this information we could check whether reassurance of the patient as reported by the GP was really perceived as reassurance by the patient.

In total, 430 patients of 18 years or older were referred for upper abdominal US. Patient management plans for 35 patients (8%) were not filled in by the GP before and/or after abdominal US. These patients were excluded from the study, resulting in a study population of 395 patients. Their patient characteristics were comparable with the included patients.

The primary outcome measure for our study was the proportion of patients in whom there was a change in anticipated patient management by the GP following upper abdominal US. This proportion and the corresponding 95% confidence interval were calculated using the statistical program Confidence Interval Analysis.[6] Additionally, subgroup analyses were performed to assess whether the patient and GP characteristics influenced the proportion of change in anticipated patient management. Associations were tested with chi-squared tests and regarded as significant when the p-value was ≤ 0.05. Data were analysed using SPSS for Windows version 11.0.

Results

Mean age of the patients at time of the abdominal US was 54 years (sd 15.8) and 35% were male. Ten percent of the patients had a prior diagnosis of cholelithiasis or nephrolithiasis and 7% had a prior cholecystectomy. Almost 80% of the patients had complaints of abdominal pain. Abnormalities with physical examination were found in 44% of the patients. The most common suspected diagnosis was cholelithiasis (47%) and nephrolithiasis (13%) (Table 1).

The radiology reports of abdominal US showed no abnormality in 269 patients (68%) and follow-up of an abnormality detected previously on abdominal US in 12 patients (3%). Clinically relevant abnormalities were found in 114 abdominal US (29%), these included: malignancy (n=9; 2%), cholelithiasis (n=74; 19%), nephrolithiasis (n=7; 2%), and other clinically relevant abnormalities that required further investigation according to the radiologist (n=24; 6%). Five of the 9 malignancies were detected in the liver, 3 in the pancreas, and 1 in the kidney. The other clinically relevant abnormalities were: 8 solid lesions of the liver, 6 other abnormalities of the kidney (e.g. large cysts), 3 gallbladder polyps, 3 abnormalities of the bowels (e.g. Crohn disease), 1 AAA, 1 umbilical hernia, 1 patient with small nodular lesions of the spleen, and 1 patient with ascitis.

As expected, all patients with a malignancy were referred to medical specialists after abdominal US. Fifty-two patients (70%) with cholelithiasis and 2 patients (29%)

TABLE 1. Patient characteristics (n=395)

	n (%)
Age (mean ± sd in years)	54.0±15.8
Gender (male)	139 (35)
Cholecystectomy in medical history	27 (7)
Prior diagnoses	
Malignancy	16 (4)
Cholelithiasis/Nephrolithiasis	40 (10)
History taking	
Abdominal pain	308 (78)
Haematuria	16 (4)
Abnormalities defecation	26 (7)
General complaints	
Weight loss	19 (5)
Nausea/vomiting	50 (13)
General malaise	37 (9)
Abnormalities with physical examination*	172 (44)
Frequent suspected diagnoses before US	
Cholelithiasis	184 (47)
Nephrolithiasis	50 (13)
Pathology liver	37 (9)
Irritable bowel syndrome	36 (9)
Unspecified pathology gallbladder	26 (7)

* A physical examination was considered abnormal when abnormalities were detected with auscultation (e.g. increased bowel sounds), percussion (e.g. dullness), or palpation (e.g. pain)

with nephrolithiasis were referred to a medical specialist by their GP after abdominal US. Noticeable was that 16 patients (4%) with no abnormalities detected on the abdominal US were referred to a medical specialist. In ten patients the GP was not able to come to a diagnosis after abdominal US and they were referred to a medical specialist for further diagnostic workup, and in six patients the suspected diagnosis of the GP was confirmed by exclusion of other pathology and these patients were subsequently referred to a specific medical specialist, e.g. gastroenterologist.

The proportion of patients in whom upper abdominal US resulted in a change in anticipated patient management was 64% (95% CI 59%-68%). Main changes in patient management plans after abdominal US included: a reduction in anticipated referrals to a medical specialist from 179 (45%) to 119 (30%); and more frequent reassurance of the patient, from 58 (15%) to 170 (43%) patients (Table 2).

TABLE 2. Patient management plans of general practitioners before and after upper abdominal ultrasound

BEFORE(n) / AFTER (n (%))	Referral medical specialist	Therapeutic management	Reassurance	Follow-up by GP*	Total
Referral medical specialist	**71 (40)**	19 (43)	7 (12)	22 (19)	119† (30)
Therapeutic management	13 (7)	**4 (9)**	4 **(7)**	7 (6)	28 (7)
Reassurance	66 (37)	13 (30)	**37 (64)**	54 (48)	170† (43)
Follow-up by GP*	29 (16)	8 (18)	10 (17)	**31 (27)**	78† (20)
Total	179 (45)	44 (11)	58 (15)	114 (29)	395

* Follow-up by GP: predominantly watchful waiting or additional diagnostic testing, such as gastroscopy or laboratory investigation

† The differences in proportions of patient management after abdominal US were significant with a p-value ≤ 0.05

The proportion of patients in whom abdominal US resulted in a change in the anticipated patient management was significantly higher in patients with a negative US finding, compared to patients with a clinically relevant finding on abdominal US, 72 % (95% CI 68%-76%) and 43% (95% CI 36%-51%) respectively. Subgroup analyses revealed that the proportion of patients in whom the patient management changed after upper abdominal US was significantly higher among patients with a prior cholecystectomy (82%) (Table 3). This was mainly caused by a larger decline of anticipated referrals to a medical specialist after abdominal US (from 48% to 22%), because no abnormalities were detected with the US examination in almost 90% of these patients. None of the other patient characteristics influenced the proportion of management changes. The characteristics of the GPs (solo or group practice, gender and year of graduation) had little influence on the proportion of change in management of 64%.

TABLE 3. Proportion of changes in patient management after upper abdominal US in relevant subgroups

	Change in management	
	n	%
All patients	252	64
Age		
< 55 years	138	66
≥ 55 years	114	61
Gender		
Male	89	64
Female	163	64
Cholecystectomy in medical history	22	82*
Prior diagnoses		
Malignancy	8	50
Cholelithiasis/Nephrolithiasis	28	70
History taking		
Abdominal pain	201	65
Abnormalities defecation	19	73
Nausea/vomiting	30	60
Abnormalities with physical examination†	110	64
Suspected diagnosis cholelithiasis according to GP	115	63
Suspected diagnosis nephrolithiasis according to GP	30	60

* $p \leq 0.05$
† A physical examination was considered abnormal when abnormalities were detected with auscultation (e.g. increased bowel sounds), percussion (e.g. dullness), or palpation (e.g. pain)

Almost one-third of the patients who returned the questionnaire reported that abdominal US had no consequences for him/her. In total 46% of the patients with a negative finding on abdominal US felt reassured by the US. It was noted that 37% of the 170 patients who were reportedly reassured by their GP after abdominal US failed to perceive the result of the US as reassurance.

Discussion

The proportion of patients for whom the anticipated patient management changed following upper abdominal US was 64%. Main changes included: fewer intended referrals to a medical specialist (from 45% to 30%); and more frequent reassurance of the patient (from 15% to 43%).

To our knowledge this is the first study that has investigated the influence of upper abdominal US on patient management in general practice. The studies of Charlesworth et al[2], Colquhoun et al[3], Connor et al[4], and Mills et al[5] reported numbers of clinically relevant abnormalities in 25%, 30%, 28% and 27%, respectively, of patients referred for abdominal US by GPs. The 29% clinically relevant abnormalities found in our study is comparable. In addition, our study showed that the full value of upper abdominal US cannot be assessed in terms of positive findings alone. Negative findings are important for exclusion of diseases and, therefore, for reassurance of the patient. However, such findings can also result either in referral of patients to a medical specialist for further evaluation of their complaints when an abdominal US fails to show any abnormalities, or in the referral of patients to a suitable medical specialist, when specific pathology is excluded.

Subgroup analyses revealed that the proportion of patients in whom patient management changed after upper abdominal US was significantly higher among patients with a prior cholecystectomy (82%). This was mainly caused by a larger decline of anticipated referrals to a medical specialist after abdominal US. Obviously, in those patients hidden postcholecystectomy gallstone pathology was excluded by the absence of choledochus dilatation or intrahepatic stones.

Over 80% of the questionnaires were returned by the patients, which increased the validity of these results. It was noted that almost 40% of the 170 patients who were reportedly reassured by their GP after abdominal US failed to perceive the result of the US as reassurance. Therefore, it seems abdominal US did not have much value for these patients, because no referral or treatment followed after the radiological investigation and reassurance was not achieved.

Before we can reach a conclusion, it is important to note that this study has several limitations. It was impossible to verify whether or not the GP really would have conducted the anticipated patient management in accordance with the plan made on the standardized form before abdominal US was performed. This could result in an overestimation of intended referrals to medical specialists. Furthermore, this study does not prove that the patient actually benefits from the diagnostic procedure, e.g. in terms of morbidity, mortality or quality of life. However, the study is the first to show that the procedure often leads to changes in anticipated patient management, which is one of the prerequisites for successfully influencing clinically relevant patient outcomes.

In conclusion, the GP's anticipated patient management strategy was changed for 64% of patients following upper abdominal US. Abdominal US substantially reduced the number of intended referrals to a medical specialist and more patients could be reassured by their GP.

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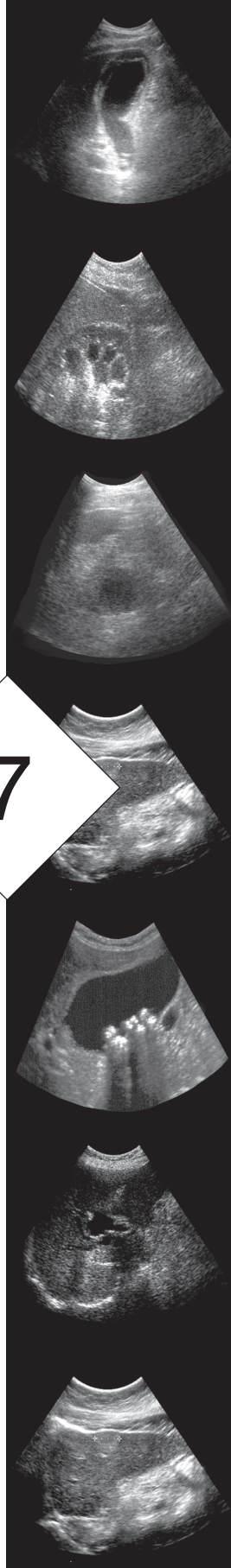
Expected and unexpected gallstones in primary care



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Speets AM, Van der Graaf Y, Hoes AW, Kalmijn S, De Wit NJ, Mali WPThM. Expected and unexpected gallstones in primary care. Submitted.

Abstract

Background. This prospective cohort study assessed the differences in signs and symptoms of primary care patients with expected and unexpected gallstones referred for upper abdominal ultrasound (US).

Methods. 430 patients aged ≥ 18 years were referred by 76 general practitioners (GPs) for abdominal US to one of the three participating hospitals in The Netherlands. All GPs were asked to fill in a standardized questionnaire before and after abdominal US. Patients with expected gallstones had a clinical suspicion of gallstones and cholelithiasis on abdominal US, patients with unexpected gallstones had cholelithiasis without a clinical suspicion.

Results. Almost 50% of the patients were referred for abdominal US because of a clinical suspicion of gallstones. Cholelithiasis was detected with US in 29% of the patients with, and 11% without a clinical suspicion of gallstones. In patients suspected of gallstones, patients with cholelithiasis on US were significantly less often male, had no prior cholecystectomies, more often colicky pain, and were more frequently referred to a medical specialist after US. Patients with unexpected gallstones were more often male, had less complaints of upper abdominal and colicky pain, and were less frequently referred to a medical specialist after US, compared to patients with expected gallstones.

Conclusion. Gallstones were detected with upper abdominal US in 29% of the patients with, and 11% without a clinical suspicion of gallstones. This study showed marked differences in signs and symptoms of patients suspected of gallstones with and without cholelithiasis detected on abdominal US, and in patients with expected and unexpected gallstones.

Introduction

The mean prevalence of gallstones reported in European populations is 10-12%. This prevalence increases with increasing age, female gender, obesity, heredity and fertility.[1] Gallstones exist in three clinical stages: asymptomatic, symptomatic (e.g. biliary colic), and complicated. About 1% of the asymptomatic patients will become symptomatic each year.[2] A general clinical guideline is that asymptomatic patients should not undergo cholecystectomy until symptoms develop.[2] Non-specific symptoms, such as dyspepsia and intolerance of fatty food, are not indicative of cholelithiasis, but are commonly reported in patients with gallstones.[3]

Abdominal ultrasound is an important diagnostic imaging method for detecting gallstones. Abdominal US provides more than 95% sensitivity and specificity for the diagnosis of gallstones greater than 2 mm in diameter, can evaluate the condition of the gallbladder (e.g. thickening of the gallbladder wall) and the diameter of the choledochus duct (indicative of obstruction), and has the ability to examine adjacent organs.[2-4] Four retrospective studies demonstrated that gallstones were detected with abdominal US in 18-24% of the patients with a clinical suspicion of gallstones, and unexpected gallstones were found in 9% of the patients without a clinical suspicion of gallstones.[5-8] Although abdominal US is frequently used for diagnosing cholelithiasis, evaluations of abdominal US in patients with abdominal complaints referred by general practitioners (GPs) have scarcely been reported in the scientific literature.

The objective of this prospective cohort study was to assess 1) the determinants of cholelithiasis in primary care patients referred for upper abdominal US because of a clinical suspicion of gallstones, and 2) the differences in signs and symptoms in patients with expected and unexpected gallstones on abdominal US.

Methods

This prospective cohort study was conducted from April 2003 to December 2004 with the help of 76 GPs participating in the catchment area of one of three general hospitals located in three main cities in The Netherlands (Jeroen Bosch Hospital in 's-Hertogenbosch; Gelre Hospitals in Apeldoorn; 'Onze Lieve Vrouwe Gasthuis' in Amsterdam). All patients of 18 years and older who were referred for upper abdominal US by their GP to one of these hospitals were included in the study, resulting in a study population of 430 patients. The study was approved by the Medical Ethics Review Board.

All GPs were asked to fill in a standardized questionnaire before requesting an abdominal US, including information on history, physical examination, indication, clinical suspicion with estimated prior probabilities on a visual analogue scale (range 0-100%), and anticipated patient management. The management options included: referral to a medical specialist; medication prescription; reassurance of the patient; and follow-up by the GP (watchful waiting or additional diagnostic testing). After the GP received the report (within 1-4 days after the US) he or she filled in a second questionnaire, again including the clinical suspicion with estimated posterior probabilities, and anticipated patient management plan.

The findings on upper abdominal US were categorized into three groups: (1) cholelithiasis; (2) other clinically relevant abnormalities; (3) no abnormality. Six months after the abdominal US a short questionnaire was sent to all patients (response rate 81%), in order to evaluate their current complaints and assess the value and consequences of abdominal US according to the patient.

The GPs could fill in three probable diagnoses on the standard questionnaire before requesting an upper abdominal US. All patients who were referred for abdominal US with a clinical suspicion of cholelithiasis as one of these probable diagnoses were classified as patients with a clinical suspicion of cholelithiasis by the GP before US (n=198). Subsequently, the patients were divided in four different subgroups, based on probability of cholelithiasis and the presence of cholelithiasis on abdominal US: 1) patients with a clinical suspicion of gallstones and cholelithiasis on abdominal US, i.e. expected gallstones; 2) patients with a clinical suspicion of gallstones without cholelithiasis on US; 3) patients without a clinical suspicion of gallstones and cholelithiasis on abdominal US, i.e. unexpected gallstones; 4) patients without a clinical suspicion of gallstones and without cholelithiasis on abdominal US. The patient characteristics of patient group 2 and 3 were compared with group 1, and analyzed with chi-squared tests. Statistical significance was inferred when the p-value was equal to or less than 0.05. Data were analysed using SPSS for Windows version 11.0. In addition, the positive predictive value of a gallstone diagnosis by the GP (percentage patients with gallstones on abdominal US in the patient group with a clinical suspicion of cholelithiasis), and the negative predictive value of no gallstone diagnosis by the GP (percentage patients without gallstones on abdominal US in the patient group without a clinical suspicion of cholelithiasis) were calculated.

TABLE 1. Patient characteristics (n=430)

	n (%)
Age (mean ± sd in years)	53.5±15.9
Gender (male)	155 (36)
Medical history	
Cholecystectomy	29 (7)
Prior diagnoses	
Malignancy	16 (4)
Cholelithiasis	33 (8)
History taking	
Upper abdominal pain	213 (50)
Colicky pain	92 (21)
Radiating pain to back, flank or shoulders	91 (21)
Abnormalities defecation	28 (7)
Nausea/vomiting	55 (13)
General malaise	41 (10)
Physical examination	
Abnormalities during percussion	28 (7)
Abnormalities during palpation	161 (37)
Frequent suspected diagnoses before abdominal US	
Cholelithiasis	198 (46)
Nephrolithiasis	51 (12)
Pathology liver	37 (9)
Irritable bowel syndrome	37 (9)
Unspecified pathology gallbladder	26 (6)

Results

The mean age of the patients was 53.5 years (sd 15.9 years), and 36% were male. Eight percent of the patients had a prior diagnosis of cholelithiasis and 7% a cholecystectomy. Upper abdominal pain was the most frequently reported symptom among the patients (50%). Colicky pain was reported in 21% of the patients. Abnormalities during percussion and palpation were found in respectively 7% and 37% of the patients. In total, 198 patients (46%) were referred for upper abdominal US with a clinical suspicion of gallstones, and the remaining 232 patients (54%) with suspected diagnoses such as nephrolithiasis (Table 1).

TABLE 2. Signs and symptoms of four subgroups patients, based on probability of cholelithiasis and the presence of cholelithiasis on upper abdominal ultrasound

	Clinical suspicion cholelithiasis by GP before US (n=198)		No clinical suspicion cholelithiasis by GP before US (n=232)	
	Cholelithiasis on US (n=58) n (%)	No cholelithiasis on US (n=140) n (%)	Cholelithiasis on US (n=25) n (%)	No cholelithiasis on US (n=207) n (%)
Age				
< 40 years	14 (24)	40 (29)	4 (16)	36 (17)
40-60 years	25 (43)	67 (48)	10 (40)	84 (41)
> 60 years	19 (33)	33 (24)	11 (44)	87 (42)
Gender (male)	7 (12)	42 (30)*	14 (56)*	92 (44)
Cholecystectomy in medical history	0	12 (9)*	0	17 (8)
Prior diagnosis of cholelithiasis	3 (5)	13 (9)	0	17 (8)
History taking				
Upper abdominal pain	46 (79)	107 (76)	6 (24)*	54 (26)
Colicky pain	28 (48)	36 (26)*	6 (24)*	22 (11)
Radiating pain	10 (17)	29 (21)	7 (28)	45 (22)
Nausea/vomiting	10 (17)	34 (24)	1 (4)	10 (5)
General malaise	3 (5)	14 (10)	3 (12)	21 (10)
Physical examination				
Abnormalities during percussion	4 (7)	8 (6)	3 (12)	13 (6)
Abnormalities during palpation	29 (50)	60 (43)	10 (40)	62 (30)

* Differences in proportions of these variables compared to the patient group with a probable diagnosis of gallstones and cholelithiasis on abdominal US were statistically significant

Cholelithiasis was detected with upper abdominal US in 58 patients (29%) who were referred for US with, and in 25 patients (11%) who were referred without a clinical suspicion of cholelithiasis. Additionally, in 9 of the 58 patients with expected gallstones (16%) additional signs of cholecystitis were detected: 4 patients with a dilatation of the bile ducts, 4 patients with thickening of the gallbladder wall, and 1 patient with unspecified cholecystitis. Other clinically relevant abnormalities were found in 12 of the 140 patients (9%) suspected of gallstones, without cholelithiasis on abdominal US, and in 30 of the 207 patients (14%) without a clinical suspicion of gallstones and without cholelithiasis on US (Table 3).

TABLE 3. Findings on abdominal ultrasound, patient management after ultrasound, and follow-up of the patients after 6 months of four subgroups patients, based on probability of cholelithiasis and the presence of cholelithiasis on upper abdominal ultrasound

	Clinical suspicion cholelithiasis by GP before US (n=198)		No clinical suspicion cholelithiasis by GP before US (n=232)	
	Cholelithiasis on US (n=58) n (%)	No cholelithiasis on US (n=140) n (%)	Cholelithiasis on US (n=25) n (%)	No cholelithiasis on US (n=207) n (%)
Findings on upper abdominal US				
Cholelithiasis	58 (100)	0	25 (100)	0
Additional signs of cholecystitis	9 (16)	2 (1)	0	2 (1)
Other clinically relevant abnormalities	0	12 (9)†	0	30 (14)‡
No abnormalities	0	128 (91)	0	177 (86)
Patient management after US				
Referral medical specialist	47 (83)	19 (14)*	9 (36)*	50 (24)
Medication prescription	1 (2)	24 (18)*	2 (8)	7 (3)
Reassurance	3 (5)	67 (50)*	7 (28)*	100 (48)
Follow-up by GP§	6 (11)	25 (19)	4 (16)	43 (21)
Follow-up patients after 6 months				
Questionnaire returned by the patients	47 (81)	108 (77)	19 (76)	174 (84)
Complaints diminished or disappeared	41 (87)	69 (64)*	11 (58)*	111 (64)
Abdominal US no value for patient	1 (2)	39 (36)*	6 (32)*	58 (33)

* Differences in proportions of these variables compared to the patient group with a probable diagnosis of gallstones and cholelithiasis on abdominal US were statistically significant

† 1 malignancy (pancreas), 4 solid lesions of the liver, 3 gallbladder polyps, 1 umbilical hernia, 1 nephrolithiasis, 1 ascitis and 1 small nodular lesions of the spleen

‡ 10 malignancies (6 liver, 3 pancreas, 1 kidney), 4 solid lesions of the liver, 6 nephrolithiasis, 6 other abnormalities of the kidney (e.g. large cysts), 3 abnormalities of the bowels (e.g. Crohn disease), and 1 AAA

§ Predominantly watchful waiting or additional diagnostic testing, such as a laboratory investigation

The mean age of the 58 patients (29%) with expected gallstones was 52.8±17.0 years, and 12% were male. Almost 50% of these patients had complaints of colicky pain. In patients suspected of gallstones, patients with cholelithiasis on US were significantly less often male, had no prior cholecystectomies, and had more frequently complaints of colicky pain compared to the 140 patients without cholelithiasis on abdominal US (Table 2). After the abdominal US, the GPs referred 47 patients

(83%) to a medical specialist; 46 patients to the department of surgery, and 1 patient to the department of internal medicine. Six months after the abdominal US the current complaints were diminished or disappeared in almost 90% of the patients with expected gallstones, and only 2% reported that abdominal US had no value for him/her (Table 3).

The mean age of the 25 patients (11%) with unexpected gallstones was 59.4±15.8 years, and 56% were male. Most unexpected gallstones were detected in the patients aged older than 60 years. Six of the 25 patients (24%) had colicky pain with a clinical suspicion of nephrolithiasis. Compared to the patients with expected gallstones, the percentage males was much higher and complaints of upper abdominal pain and colicky pain occurred significantly less frequent (Table 2). The GPs referred 9 patients (36%) to a medical specialist; 3 patients to the department of surgery, and 6 patients to the department of internal medicine. Six months after the abdominal US current complaints were diminished or disappeared in almost 60% of these patients. One third of the patients reported that abdominal US had no value for him/her (Table 3).

The positive predictive value of a gallstone diagnosis by the GP was 58/198=29%. The negative predictive value of no gallstone diagnosis by the GP was 207/232=89%.

Discussion

Almost half of the primary care patients referred for upper abdominal US by their GP had a clinical suspicion of gallstones. Cholelithiasis was detected with upper abdominal US in 29% of the patients who were referred for US with, and 11% of the patients who were referred without a clinical suspicion of cholelithiasis. Gallstones were found in 18-24% of patients referred for abdominal US with a clinical suspicion of cholelithiasis in four retrospective studies.[5-8] The percentage of patients with unexpected gallstones (11%) corresponds well with the 9% unexpected gallstones found by Colquhoun et al[6] and Mills et al.[8]

A marked difference between these two patient groups was that the percentage males in the group with unexpected cholelithiasis was almost 5 times as high as in the patient group with expected gallstones. The percentage of males was also much higher (2.5 times higher) in the group patients suspected of gallstones, but without signs of cholelithiasis on abdominal US. It is widely known that the prevalence of gallstones is higher in females than in males. GPs may sooner suspect gallstones in female patients with complaints suggestive of gallstones and formulate a clinical suspicion of cholelithiasis when referring them for upper abdominal US, resulting

in a higher percentage of unexpected gallstones in males. In addition, the clinical suspicion in males with colicky pain is directed more often by GPs to kidney stones than to cholelithiasis. It was peculiar in our study that 6 patients with unexpected gallstones had complaints of colicky pain, while the GP thought cholelithiasis was unlikely; the GPs thought these complaints were caused by nephrolithiasis. None of these patients were referred to a medical specialist after abdominal US.

The number of prior cholecystectomies differed significantly in patients suspected of gallstones with and without cholelithiasis on abdominal US. Twelve patients without cholelithiasis and none of the patients with cholelithiasis had a prior cholecystectomy. It was obvious that these 12 patients were referred for an upper abdominal US with again a clinical suspicion of cholelithiasis (in the choledochus duct), and in none of them gallstones were detected with abdominal US, though choledochus or hepatic stones may have passed. It is questionable whether gallstones were the cause of the complaints in these patients, because after cholecystectomy they were referred once more for an abdominal US with complaints suspected of cholelithiasis.

The percentage of patients with unexpected gallstones referred to a medical specialist (36%) was significantly lower than the 83% patients referred with expected gallstones. Six months after the abdominal US the questionnaire revealed that in patients with unexpected gallstones the abdominal complaints less often had disappeared; patients with expected gallstones reported 6 months after the US that the current complaints were diminished or disappeared in almost 90% of the patients, compared to almost 60% of the patients with unexpected gallstones. Maybe a larger part of the abdominal complaints would have disappeared when these patients were referred to a medical specialist. Although less specific, the abdominal complaints of the patients with unexpected gallstones could have been caused by the gallstones. On the other hand, most patients with expected gallstones were referred to a medical specialist, often regarded as the best possible treatment by patients in general practice, which will have a positive effect on the perception of their complaints.

A limitation of our study is that part of the unexpected gallstones may have been classified as unexpected in our study, because the GP did not fill in a clinical suspicion of cholelithiasis before referral for abdominal US. Some patients with unexpected gallstones were referred for upper abdominal US with abdominal complaints that could be suggestive of gallstones, such as colicky pain. This could result in an underestimation of the differences between the patient groups with expected and unexpected gallstones.

In conclusion, gallstones were detected with upper abdominal US in 29% of the patients with, and 11% without a clinical suspicion of gallstones. This study showed marked differences in patients suspected of gallstones with and without cholelithiasis detected on abdominal US, and in patients with expected and unexpected gallstones.

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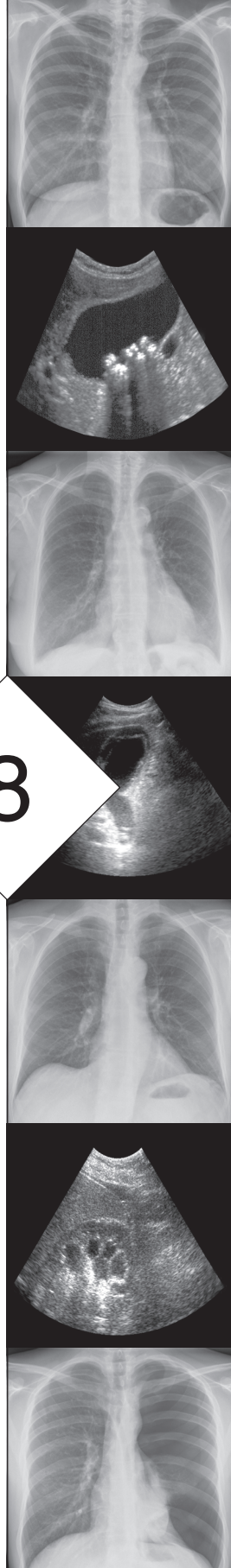
Evaluation of routinely used diagnostic tests

8



In this chapter, several methodological issues pertaining to the evaluation of the value of diagnostic tests that are frequently applied in clinical practice for a wide variety of complaints, such as chest radiography (CXR) and abdominal ultrasound (US) will be discussed.

Phases in diagnostic research

Diagnostic research is pragmatic research with the aim to optimize the diagnostic process in clinical practice. The diagnostic process is a multivariable and consecutive process of estimating the diagnostic probability of the presence of a particular disease given combinations of test results. The evaluation of a diagnostic test can be summarized in a four phase hierarchical model, comparable with the four phases of pharmaceutical research.[1,2]

Phase I consists of the test development. In diagnostic imaging studies this phase is generally the purview of physicists, and includes parameters such as sharpness, contrast and resolution.[3] The diagnostic accuracy of the test, i.e. the ability of a test to discriminate between diseased and non-diseased persons, is assessed in phase II. The discrimination capacity of the diagnostic test will be compared with results of a reference test, and is summarized in measures such as sensitivity and specificity. Phase III estimates the clinical effectiveness of the diagnostic test. Some authors[3-7] have subdivided this phase in three different levels: diagnostic impact (i.e. the influence of the test on the clinician's confidence of a diagnosis), therapeutic impact (i.e. initiation, change, or withdrawal of planned therapy), and impact on the patient outcome (e.g. influence on the health status of patients or quality of life). Phase IV of diagnostic research goes beyond the individual risks and benefits to a broader societal perspective, such as cost-effectiveness analyses.

Importance of phase III diagnostic research

Diagnostic research in phase I and II often have straightforward study designs, and most new diagnostic investigations are implemented immediately after phase II. However, the results of phase II research, summarized in measures such as sensitivity, specificity, and likelihood ratios have important limitations[8]: they do not allow for direct diagnostic interpretation, and a high sensitivity and specificity are no guarantee for diagnostic, let alone therapeutic, impact, or influence on patient outcome. Such studies of diagnostic accuracy can neither evaluate the value of the

test in the presence of other diagnostic tools, nor assess the influence on the anticipated patient management. In addition, such diagnostic studies often compare test results in a group of patients with well-established disease (i.e. more advanced stages) with a group of healthy volunteers, whereas a diagnostic test should be helpful in recognizing disease in the domain of patients suspected of the disease in everyday clinical practice. Therefore, phase II diagnostic research can be seen as just a preliminary assessment of a diagnostic test. A reason often adduced to avoid phase III diagnostic research is the fast evolution of diagnostic techniques and the alleged uniqueness of the novel test. This could be a valid argument in case of a novel test capable of providing images with undisputed therapeutic consequences in a relatively rare (suspected) disease, where no alternative techniques are available. Under these circumstances phase III and IV studies will be difficult to perform. Similar issues play a role in the less stringent way the value of orphan drugs for rare diseases is assessed. However, tests such as CXR and abdominal US are widely used in a variety of complaints and to diagnose a range of diseases and were developed many years ago. Phase II studies on the diagnostic accuracy of these tests were already performed in respectively the fifties[9-11] and end of the sixties[12-15]. Nowadays, patients are still referred frequently for these imaging investigations by general practitioners (GPs), but their added clinical value in general practice has not been sufficiently established. Clearly, more emphasis on phase III studies to determine the clinical value of these tests is required.

Study designs phase III diagnostic research

Too few studies on the clinical effectiveness of diagnostic tests have been performed in clinical practice, in particular with regard to diagnostic imaging. A cross-sectional design, which uses a “gold standard” or reference test for the identification of disease and non-disease, and including a series of consecutive patients suspected of a certain disease in daily clinical practice, is regarded as the optimal study design for phase III diagnostic research. In such studies, two multivariate models are often compared; one model with all information from patient history and physical examination, and a second model with all information from model one and the result of the additional diagnostic test. By comparing the areas under both ROC curves, the additional value of the diagnostic test can be then determined. An alternative study design is the randomized controlled trial (RCT). In a RCT patients requiring the diagnostic test under study according to the clinician will randomize for the diagnostic test. Patient management, and sometimes patient outcome, will

be compared in patients with and without the diagnostic test. Although both study designs are suitable for research in new diagnostic tests, difficulties arise in routinely used tests. The disadvantages of the cross-sectional study and RCT for diagnostic tests, such as CXR and abdominal US, routinely used in a wide range of patients to determine the presence of a variety of diseases, will be outlined in next paragraphs and an alternative design, the prospective cohort study, will be discussed.

Cross-sectional study

Primary care patients referred for CXR and upper abdominal US are a very heterogeneous patient population in which the GPs judge an additional diagnostic test necessary for further examination. The patients have a broad range of complaints, the indications for the tests vary widely, and many different diseases can be detected with these imaging investigations. In view of this, no "gold standard" or reference test is available for both routinely used diagnostic tests, and this impedes the use of a cross-sectional design to examine their clinical effectiveness. It is possible to use an expert panel to identify disease and non-disease based on all available data, preferably without the diagnostic test under evaluation to prevent incorporation bias, but (notably because of the latter), this would result in a less valid identification of disease. Moreover, a cross-sectional design is particularly suited when the clinical consequences of the, in this case multiple, diagnoses are known (such as anticoagulants in established deep vein thrombosis or surgery in certain fractures) but the consequences for many of the diagnoses established through CXR or abdominal US, such as gallbladder stones, are not unequivocal. In circumstances where a valid reference test is lacking, researchers may choose a longitudinal design, usually a RCT or prospective cohort study, in which, typically, the effect of the test on patient management or patient outcome is determined.

Randomized Controlled Trial

RCTs are not often applied in diagnostic research, for reasons such as complex logistics, the need for large sample sizes to show statistically significant differences, and high costs. In view of the multiple indications and possible diagnoses involved when a CXR or abdominal US is ordered, this may pose insurmountable problems. Designing a RCT to assess the clinical effectiveness of a routinely used diagnostic test becomes even more difficult because of ethical considerations. Ethical issues will arise when an established diagnostic test will be withheld in half of the patients.

Even if Medical Ethics Review Boards approve of such a study, most clinicians, and probably patients, will be hesitant to participate when full access to the diagnostic test is denied during the (relatively long) study period. It should be emphasized that the primary care physician, on the basis of signs and symptoms, already selected the relevant clinical domain, i.e. those patients in whom the diagnostic test is considered to provide potentially useful additional information. If, alternatively, clinicians were asked to identify patients in whom the diagnostic test can be omitted without serious consequences, only few patients would be included in the study, and the generalizability of the findings to the clinically relevant patient population would be seriously hampered.

Prospective cohort study

An alternative design for assessing the clinical effectiveness of routinely used diagnostic tests is a prospective cohort study, sometimes described as a controlled observational study or clinical value study.[6,16] In a prospective cohort study the clinician's confidence of a diagnosis and anticipated patient management before and after the clinician obtains information of the diagnostic test results can be compared, and patients in whom the diagnostic test does not lead to a change in confidence or anticipated patient management can be identified. These studies have a pragmatic character. Patients will be included in the study via their clinician who requests the diagnostic test based on the medical history and physical examination of a patient. All patients will undergo the diagnostic test and clinical practice will be as usual, which allows an evaluation of the diagnostic test in its clinical context. In addition, this will minimize the workload of clinicians and enables large numbers of participating clinicians and high inclusion rates. Freedman[16] emphasized almost 20 years ago that issues such as the continuous scale of test results and the possibility of multiple diagnoses, which are difficult to accommodate in Phase II studies of diagnostic accuracy, are incorporated naturally into this study design.

An important limitation of this type of study is the fact that the clinicians assess the value of the diagnostic test by filling in the patient management before and after the test. In this way clinicians may influence the estimated value of a diagnostic test, because most clinicians will not judge their requested test as inefficient. Besides, clinicians have to fill in the anticipated patient management before the diagnostic test as if no diagnostic test would be performed. It is impossible to verify whether or not the clinician really would have conducted the anticipated

patient management in accordance with the plan made before the diagnostic test. This could result in an overestimation of the prevalence of the most invasive anticipated patient management categories, such as surgical interventions. Finally, when the outcome is change in patient management, the benefit for the patient in terms of reduction in morbidity of even mortality is not measured. This would require huge sample sizes and long-term follow up periods, and these studies are hardly feasible, notably in the broad patient domain indicated for CXR or abdominal US.

Conclusion

Diagnostic research in phase I and II is essential for the development of a new diagnostic test. These studies often have straightforward study designs, and most new diagnostic tests are implemented immediately after phase II. However, such diagnostic accuracy research can be seen as just a preliminary assessment of a diagnostic test. The next phase, the assessment of the clinical effectiveness of a new test in daily practice, is more complicated and only conducted in a small percentage of the new diagnostic tests. Phase III diagnostic research in routinely used diagnostic tests is even more complicated, because the standard study design (cross-sectional study with a reference test) and a RCT are usually not feasible, and is therefore seldom performed. A prospective cohort study, in which the anticipated patient management of the clinician is compared before and after the test, offers an alternative study design. Despite the limitations of such studies, they provide a pragmatic and valid way to assess the effectiveness of diagnostic tests routinely applied in clinical practice in many patients with a wide range of complaints and possible indications.

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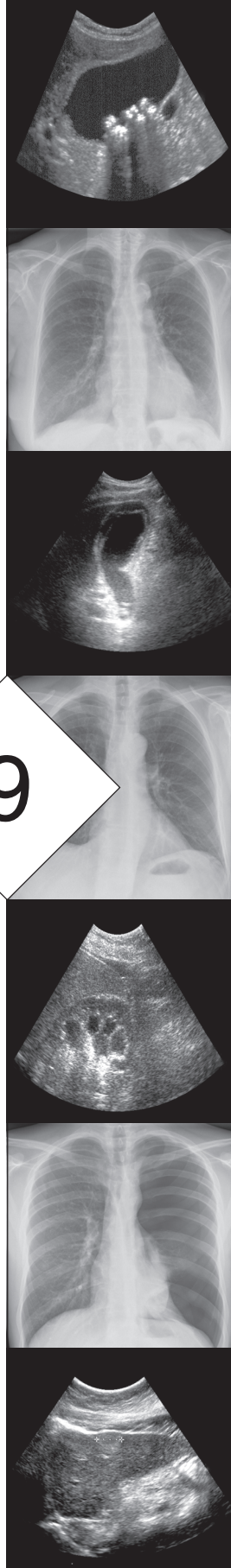

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Chapter 1 includes a short introduction of the diagnostic process and introduces two of the most widely used diagnostic imaging techniques in Western societies, chest radiography (CXR) and abdominal ultrasound (US). The main objective of this thesis, to determine the clinical effectiveness of CXR and upper abdominal US in general practice, and the objectives of the studies presented in the subsequent chapters were described in this chapter.

In Chapter 2 the study based on data of the Health Insurance Company Agis in The Netherlands from 1999 to 2003 was described. This study provided detailed information on the number of CXR and abdominal US examinations by age, gender, referring physician and ethnicity. CXRs were ordered in 130 per 1000 persons per year, and abdominal US examinations in 39 per 1000 persons per year. These frequencies did not change noticeable over the period 1999 to 2003. CXR was performed significantly more often in males, and abdominal US significantly more often in females. The frequencies of both imaging examinations were highest in persons aged 70-79 years. General practitioners (GPs) more frequently referred younger patients and females, especially for abdominal US, compared to medical specialists. Up to the age of 60 years the frequencies of both CXR and abdominal US were higher in Turks and Moroccans compared to other nationalities.

Chest radiography

The influence of CXR on patient management in general practice was studied in Chapter 3. In total, 792 patients aged ≥ 18 years referred by 78 general practitioners (GPs) for CXR to one of the three participating hospitals in The Netherlands were included in this prospective cohort study. The main outcome was change in anticipated patient management assessed by means of questionnaires filled in by GPs before and after CXR. Clinically relevant abnormalities were found in 24% of the CXRs. Anticipated patient management changed in 60% of the patients following CXR, and the main changes included fewer referrals to a medical specialist (from 26% to 12%), a reduction in initiation or change in therapy (from 24% to 15%), and more frequent reassurance (from 25% to 46%). A change in patient management occurred significant more frequently in patients with complaints of cough (67%), exhibited abnormalities during physical examination (69%), or a suspected diagnosis of pneumonia (68%).

In **Chapter 4** the diagnostic yield of CXR in 192 primary care patients suspected of pneumonia was evaluated. Pneumonia was diagnosed by GPs in 35 patients (18%), of whom 27 patients (14%) had a positive CXR, and 8 patients (4%) a negative CXR, however with an assumed high probability of pneumonia by the GP. CXR clearly influenced the diagnosis of pneumonia by the GP in 53% of the patients: CXR ruled out pneumonia in 47%, and the probability of pneumonia substantially increased in 6% of the patients. Anticipated patient management changed after CXR in 69% of the patients, mainly caused by a reduction in medication prescription (from 43% to 17%), and more frequent reassurance of the patient (from 8% to 35%). Therefore, CXR is an important diagnostic tool in primary care patients with a clinical suspicion of pneumonia in terms of change in the estimated probability of pneumonia, and change in anticipated patient management.

Abdominal ultrasound

In **Chapter 5** the cross-sectional study in 499 patients aged ≥ 18 years with abdominal pain referred by their GP for abdominal US to the University Medical Centre Utrecht in The Netherlands was described. Mean age at time of the US was 47.9±15.2 years, and almost one third of the patients were male. Significant pathology was seen in 81 patients (16%). Older age (OR 1.03 per year), colicky pain (OR 2.80) and a clinical suspicion of bile stones (OR 2.31) were predictors of a significant abnormal finding on abdominal US.

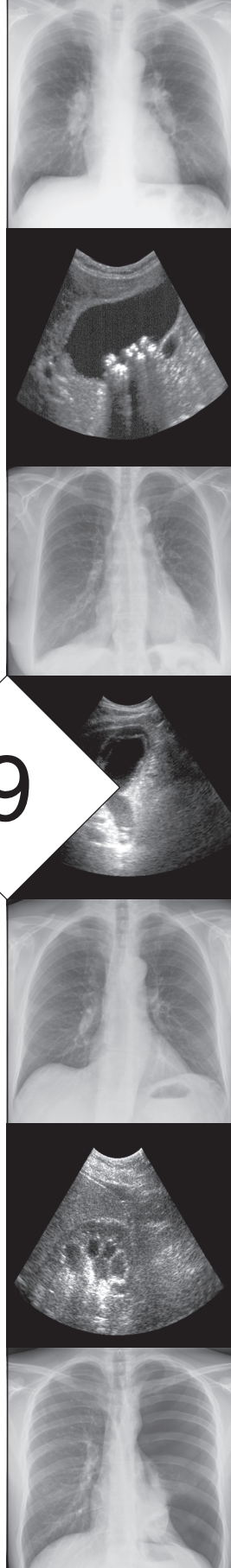
The diagnostic value of upper abdominal US in terms of changes in patient management decisions in primary care was determined in 395 patients referred for abdominal US in **Chapter 6**. The mean age of the patients was 54.0±15.8 years, and 35% were male. Clinically relevant abnormalities were found in 29% of the abdominal US, mainly cholelithiasis. Anticipated patient management changed in 64% of the patients following abdominal US. Abdominal US substantially reduced the number of intended referrals to a medical specialist (from 45% to 30%), and more patients could be reassured by their GP (from 15% to 43%). A change in anticipated patient management occurred significantly more frequently in patients with a prior cholecystectomy (82%).

The differences in signs and symptoms of 430 primary care patients with expected and unexpected gallstones referred for upper abdominal US were assessed in **Chapter 7**. 76 participating GPs were asked to fill in a standardized questionnaire

before and after abdominal US. Almost 50% of the patients were referred for abdominal US because of a clinical suspicion of gallstones. Cholelithiasis was detected with US in 29% of the patients with, and 11% without a clinical suspicion of gallstones. This study showed marked differences in signs and symptoms of patients suspected of gallstones with and without cholelithiasis detected on abdominal US, and in patients with expected and unexpected gallstones. In patients suspected of gallstones, patients with cholelithiasis on abdominal US were significantly less often male, had no prior cholecystectomies, more often colicky pain, and were more frequently referred to a medical specialist after US. Patients with unexpected gallstones were more often male, had less complaints of upper abdominal and colicky pain, and were less frequently referred to a medical specialist after US, compared to patients with expected gallstones.

In Chapter 8 several methodological issues pertaining to the evaluation of the value of diagnostic tests that are frequently applied in clinical practice for a wide variety of complaints, such as the CXR and abdominal US, were be discussed. Diagnostic research in phase I and II is essential for the development of a new diagnostic test. These studies often have straightforward study designs, and most new diagnostic tests are implemented immediately after phase II. However, such diagnostic accuracy research can be seen as just a preliminary assessment of a diagnostic test. The next phase, the assessment of the clinical effectiveness of a new test in daily practice, is more complicated and only conducted in a small percentage of the new diagnostic tests. Phase III diagnostic research in routinely used diagnostic tests is even more complicated, because the standard study design (cross-sectional study with a reference test) and a RCT are usually not feasible, and is therefore seldom performed. A prospective cohort study, in which the anticipated patient management of the clinician is compared before and after the test, offers an alternative study design. Despite the limitations of such studies, they provide a pragmatic and valid way to assess the effectiveness of diagnostic tests routinely applied in clinical practice in many patients with a wide range of complaints and possible indications.

Summary
Samenvatting
Dankwoord
Curriculum Vitae



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Hoofdstuk 1 bevat een korte inleiding over het diagnostische proces en er worden twee van de meest gebruikte diagnostische beeldvormende technieken in Westerse landen geïntroduceerd, de X-thorax en buikechografie. Het doel van dit proefschrift was om de klinische relevantie van X-thorax en buikechografie in de huisartspraktijk te bepalen. De onderwerpen van de onderzoeken beschreven in de volgende hoofdstukken van dit proefschrift worden weergegeven aan het einde van hoofdstuk 1.

In **hoofdstuk 2** wordt het onderzoek beschreven dat was gebaseerd op de data van de Zorgverzekeraar Agis uit de periode 1999 t/m 2003. In dit onderzoek werd gedetailleerde informatie over het aantal X-thorax en buikechografie onderzoeken gepresenteerd voor leeftijd, geslacht, verwijzende arts en etniciteit. Gemiddeld werden 130 per 1000 personen per jaar doorverwezen voor een X-thorax en 39 per 1000 personen per jaar voor een buikechografie. Deze frequenties wijzigden nauwelijks gedurende de periode van 1999 t/m 2003. De X-thorax werd significant vaker aangevraagd voor mannen, en buikechografie significant meer voor vrouwen. De frequenties voor beide beeldvormende onderzoeken waren het hoogst in personen met een leeftijd van 70-79 jaar. In vergelijking met specialisten verwezen huisartsen vaker jongere mensen en vrouwen door, vooral voor buikechografie. De frequenties van zowel de X-thorax als buikechografie waren hoger in mensen tot 60 jaar met een Turkse of Marokkaanse nationaliteit in vergelijking met andere nationaliteiten.

X-thorax

De invloed van de X-thorax op het huisartsenbeleid werd onderzocht in **hoofdstuk 3**. In totaal werden er 792 patiënten van 18 jaar en ouder geïncludeerd in dit prospectieve cohort onderzoek. Zij werden doorverwezen voor een X-thorax naar één van de drie participerende Nederlandse ziekenhuizen door 78 huisartsen. De primaire uitkomstmaat was de verandering in het voorgenomen beleid, vastgesteld door middel van vragenlijsten ingevuld door de huisarts voor en na de X-thorax. In 24% van de X-thorax werden klinische relevante afwijkingen gevonden. Het beleid van de huisarts veranderde in 60% van de patiënten na de X-thorax. De belangrijkste veranderingen waren een afname van de voorgenomen verwijzingen naar een medisch specialist (van 26% naar 12%), een afname van de voorgeschreven therapie (van 24% naar 15%) en een toename van het aantal gerustgestelde patiënten (van 25% naar 46%). Het beleid van de huisarts veranderde significant vaker in patiënten met hoestklachten (67%), afwijkingen tijdens het lichamelijk onderzoek (69%) of een verdenking op pneumonie (68%).

In **hoofdstuk 4** werd het diagnostische nut van de X-thorax geëvalueerd in 192 patiënten met een klinische verdenking op pneumonie. De diagnose pneumonie werd in 35 patiënten (18%) gesteld: 27 patiënten (14%) hadden een positieve X-thorax en 8 patiënten (4%) een negatieve X-thorax, maar met grote verdenking op pneumonie volgens de huisarts. De X-thorax beïnvloedde de diagnosestelling pneumonie door de huisarts in 53% van de patiënten: X-thorax sloot een pneumonie uit in 47% van de patiënten, en de waarschijnlijkheid van pneumonie nam substantieel toe in 6% van de patiënten. Het beleid van de huisarts veranderde in 69% van de patiënten na de X-thorax, vooral veroorzaakt door een afname van de voorgeschreven medicatie (van 43% naar 17%), en een toename van de geruststelling van patiënten (van 8% naar 35%). Door zijn invloed op de verandering van de waarschijnlijkheid van pneumonie en beleidsveranderingen is de X-thorax een belangrijke diagnostische test voor patiënten in de huisartspraktijk met een klinische verdenking op pneumonie.

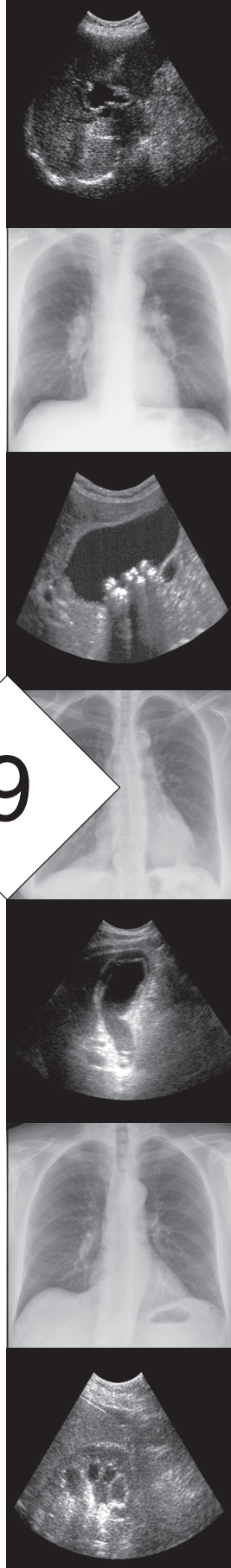
Buikechografie

In **hoofdstuk 5** wordt het cross-sectionele onderzoek beschreven dat werd uitgevoerd in het Universitair Medisch Centrum Utrecht in 499 patiënten met buikpijn van 18 jaar en ouder, doorverwezen voor buikechografie vanuit de huisartspraktijk. De gemiddelde leeftijd was 47.9±15.2 jaar, en bijna een derde van de patiënten was man. In 81 patiënten (16%) werden significante afwijkingen gevonden. Een hogere leeftijd, (OR 1.03 per jaar), koliekpijn (OR 2.80) en een klinische verdenking op galstenen (OR 2.31) waren voorspellers van een klinisch relevante afwijking op de buikechografie.

De invloed van de buikechografie op het huisartsenbeleid werd onderzocht in **hoofdstuk 6**. In totaal werden 395 patiënten doorverwezen voor buikechografie vanuit de huisartspraktijk geïncludeerd. De gemiddelde leeftijd was 54.0±15.8 jaar, en 35% van de patiënten was man. In 29% van de buikechografieën werden klinisch relevante afwijkingen gevonden, voornamelijk galstenen. Het beleid van de huisarts veranderde in 64% van de patiënten na de buikechografie. De belangrijkste veranderingen waren een afname van de voorgenomen verwijzingen naar een medisch specialist (van 45% naar 30%), en een toename van het aantal patiënten dat gerustgesteld werd door de huisarts (van 15% naar 43%). Het beleid van de huisarts veranderde significant vaker in patiënten die al eerder een cholecystectomie hadden ondergaan (82%).

De verschillen in symptomen van 430 patiënten met verwachte en onverwachte galstenen, doorverwezen voor buikechografie vanuit de huisartspraktijk werden onderzocht in **hoofdstuk 7**. 76 participerende huisartsen vulden voor en na de buikechografie een gestandaardiseerde vragenlijst in. Bijna de helft van de patiënten werd doorverwezen voor buikechografie met een verdenking op galstenen. In totaal werden in 29% van de patiënten met een verdenking op galstenen, en in 11% van de mensen zonder een klinische verdenking, galstenen gevonden met behulp van buikechografie. Dit onderzoek heeft een aantal opvallende verschillen tussen de patiëntengroepen aangetoond. Patiënten met aangetoonde galstenen op de buikechografie in de patiëntengroep verdacht van galstenen waren significant minder vaak man, hadden geen eerdere cholecystectomie ondergaan, hadden meer last van koliekpijn en werden vaker doorverwezen naar een specialist na de echografie. Patiënten met toevals galstenen waren vaker man, hadden minder last van buikpijn en koliekpijn en werden minder vaak doorverwezen naar een medisch specialist in vergelijking met patiënten met verwachte galstenen.

In **hoofdstuk 8** worden verschillende methodologische issues besproken met betrekking tot de evaluatie van de waarde van veelvuldig aangevraagde diagnostische onderzoeken voor een breed scala van klachten, zoals de X-thorax en buikechografie. Diagnostisch onderzoek in fase I en II is essentieel voor de ontwikkeling van een nieuwe diagnostische test. Deze onderzoeken hebben vaak een eenduidige onderzoeksopzet en de meeste nieuwe tests worden direct na fase II geïmplementeerd, maar de evaluatie van een diagnostische test is nog niet volledig na fase II. In de volgende fase wordt de klinische effectiviteit van een nieuwe test in de dagelijkse praktijk onderzocht. Deze fase is gecompliceerd en wordt slechts in een klein deel van de nieuwe diagnostische tests uitgevoerd. Fase III diagnostisch onderzoek in veelvuldig gebruikte diagnostische tests is nog gecompliceerder, omdat de twee basis onderzoeksopzetten (cross-sectioneel onderzoek met referentie test en RCT) niet toepasbaar zijn in deze situatie, en wordt daarom zelden uitgevoerd. Een prospectief cohort onderzoek, waarin het voorgenomen beleid van de arts voor en na de test wordt vergeleken, biedt een alternatief. Ondanks de beperkingen van een prospectief cohort onderzoek, is het een pragmatische en valide manier om de effectiviteit van een veelvuldig gebruikte diagnostische test in de dagelijkse praktijk te onderzoeken.



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Er zijn veel mensen die ik dank verschuldigd ben bij het tot stand komen van dit proefschrift. Zonder anderen tekort te doen wil ik een aantal van hen met name noemen.

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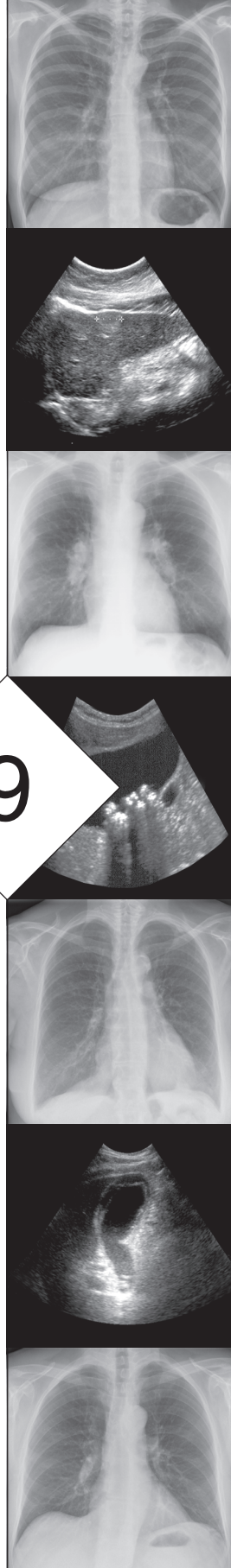

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Anouk Speets was born on October 18th, 1978 in Harderwijk, The Netherlands. After graduating secondary school at the Regionale Scholen Gemeenschap 't Slingerbos in Harderwijk in 1997, she started the study Health Sciences (with the specialization Movement Sciences) at the University of Maastricht. In 2001 she performed a research project on gait rehabilitation in spinal cord injury patients in three Dutch rehabilitation centres (supervised by Prof. dr. H. Kuipers, dr. F.T.J. Verstappen and dr. M.W.M. Post). After graduating in August 2001 she interviewed persons with a physical or multiple handicap for a research project of the Institute for Rehabilitation Research (iRv) in Hoensbroek. In July 2002, she started the research project described in this thesis at the Department of Radiology, University Medical Centre Utrecht, under supervision of Prof. dr. W.P.Th.M. Mali, Prof. dr. A.W. Hoes, Prof. dr. Y. van der Graaf and dr. S. Kalmijn. She obtained her Master of Science degree in Clinical Epidemiology at the Netherlands Institute for Health Sciences (NIHES), Erasmus Medical Centre Rotterdam in August 2004.

Anouk Speets lives together with Hans Oordt. On February 24th, 2005 their daughter Milica is born.

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