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Comorbidity in older surgical cancer patients: Influence on patient care and outcome

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ABSTRACT

Evidence is scarce about the influence of comorbidity on outcome of surgery, whereas this information is highly relevant for estimating the surgical risk of cancer patients, and for optimising pre-, peri- and postoperative care. In this paper, the prognostic role of increasing age and comorbid conditions in patients diagnosed with stage I–III colorectal, stage I–II NSCLC or stage I–III breast cancer between 1995 and 2004 in the southern part of the Netherlands is summarised.

Almost all patients with stage I–III colon cancer or rectal cancer underwent surgery regardless of age or comorbidity. In contrast, the resection rate among elderly patients with stage I–II NSCLC was clearly lower than among younger patients and was significantly lower when COPD, cardiovascular diseases or diabetes were present. Among patients with stage I–III breast cancer, those aged 80 or older underwent less surgery, and the resection rate appeared to be lower when cardiovascular diseases or diabetes were present.

Among patients with resected colorectal cancer, postoperative morbidity and mortality were higher among those undergoing emergency surgery, and also among those with reduced pulmonary function, cardiovascular disease or neurological comorbidity. Among those with resected NSCLC, postoperative morbidity and mortality were related to reduced pulmonary function or cardiovascular disease. Since surgery for breast cancer is low risk, elective surgery, morbidity and mortality were not higher for elderly or those with comorbidity.

Among patients with colorectal or breast cancer, comorbidity in general, cardiovascular diseases, COPD, diabetes (only colon and breast cancer) and venous thromboembolism had a negative effect on overall survival, whereas the effect of comorbidity on survival of stage I–II NSCLC was less clear.

Elderly and those with comorbidity (especially cardiovascular diseases and COPD) among colorectal cancer and NSCLC patients had more postoperative morbidity and mortality. Prospective randomised studies are needed for refining selection criteria for surgery in elderly cancer patients and for anticipation and prevention of complications.

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1. Introduction

Due to ageing of the population and rising incidence rates of most cancers with age, the mean age of patients diagnosed with cancer is increasing in western countries. This implies that patients increasingly suffer from one or more other serious (chronic) diseases, especially cardiovascular diseases, COPD, hypertension or diabetes.[1] Besides affecting life expectancy, comorbid conditions may complicate major surgery in cancer patients, especially when they are frail.[2–6] Surgery is the only curative treatment option for patients with colorectal cancer, stage I–II non-small cell lung cancer (NSCLC) or breast cancer. Until now, there is lacking evidence about the influence of specific comorbid conditions on outcome of surgery as these elderly patients are often excluded from clinical trials. This information, however, is highly relevant for estimating the surgical risk of cancer patients, and for optimising pre-, peri- and postoperative care. Choice for surgery is clearly different among the different tumour groups. Generally speaking, surgery for colorectal cancer is often preferable because of bleeding or obstruction and the intention to perform a curative procedure (although in a non-curative setting alternative procedures are present). Surgery among lung cancer patients is high risk surgery, and radiotherapy is an alternative. Therefore, there is a strict selection of surgery among lung cancer patients. Surgery for breast cancer is low risk, but among older patients hormonal treatment is an alternative, which means that there is a more 'elective' selection.

In this paper, we summarise our findings with respect to the prognostic role of increasing age and comorbid conditions in patients diagnosed with stage I–III colorectal, stage I–II NSCLC or stage I–III breast cancer in the registration area of the population-based Eindhoven Cancer Registry, and discuss them against the background of the literature.

2. Patients and methods

The Eindhoven Cancer Registry records data on all patients newly diagnosed with cancer in the southern part of the Netherlands, an area with 2.3 million inhabitants and only with general hospitals. Since 1993, serious comorbidity with prognostic impact has been recorded for all patients. The Charlson comorbidity index is most widely used for recording comorbidity and was validated in various studies.[7] We used a slightly modified version of this index for recording comorbidity. Comorbidity was defined as life-shortening diseases that were present at the time of cancer diagnosis (previous cancer, cardiovascular diseases, COPD, diabetes, hypertension, autoimmune diseases, rheumatoid arthritis (only severe), kidney diseases (glomerulonephritis, pyelonephritis), gastrointestinal (stomach ulcer and resection, colitis), liver diseases (cirrhosis, hepatitis), dementia and chronic infections).

Trained registry personnel extract all data from the medical records between 6 and 12 months after diagnosis. The medical record is generally regarded as the most complete source of information on the patient's past and current health status.[8]

Table 1 – General characteristics and resection rate of patients

	Stage I–III colon (N = 4911)		Stage I–III rectum (N = 2674)		Stage I–II NSCLC (N = 2385)		Stage I–III breast (N = 8501)	
	Resection rate		Resection rate		Resection rate		Resection rate	
	N	(%)	N	(%)	N	(%)	N	(%)
Age								
50–64	1243	(99)	943	(99)	832	(88)	4265	(100)
65–79	2766	(99)	1382	(96)	1377	(67)	3299	(97)
80+	891	(98)	349	(92)	176	(15)	937	(81)
Gender								
Male	2456	(99)	1564	(96)	1912	(69)		
Female	2455	(99)	1110	(96)	473	(76)	8501	(97)
Histology								
Squamous cell					1104	(69)		
Adenocarcinoma					499	(85)		
Large cell undiff.					278	(51)		
Stage								
I	956	(100)	1112	(99)			3766	(98)
II	2378	(98)	944	(93)			3894	(97)
III	1577	(99)	782	(98)			841	(90)
Comorbidity								
None	1737	(99)	1112	(97)	579	(82)	4433	(99)
One condition:	1600	(99)	855	(97)	859	(69)	2501	(96)
Cardiovascular	386	(99)	183	(95)	213	(73)	356	(92)
COPD	171	(99)	117	(97)	319	(62)	199	(98)
Diabetes	130	(99)	70	(99)	46	(63)	248	(97)
Hypertension	420	(98)	241	(98)	78	(86)	1022	(98)
Two or more	1574	(99)	707	(95)	947	(64)	1567	(91)

Patients aged 50 or older with cancer of the colon or rectum (stage I–III), NSCLC (stage I–II) or breast (stage I–III), newly diagnosed between 1995 and 2004, were included for this overview. Patients for whom no information on comorbidity was found in the medical records were excluded (9.9%). Eventually, 4911 colon, 2674 rectal, 2385 NSCLC and 8501 breast cancer patients were left for analyses.

Surgery did not include diagnostic operations. Surgery comprised appendectomy, hemicolectomy, sigmoid resection, rectosigmoid resection, low anterior resection, subtotal colectomy, total colectomy and rectum amputation for colorectal cancer, wedge excision, segment resection, bisegment resection, lobectomy, bilobectomy, pneumonectomy, sleeve resection and carina resection for NSCLC, and breast conserving surgery and mastectomy for breast cancer.

Postoperative complications were studied in a random sample of resected patients (colon stage I–III $N = 223$, rectum stage I–III $N = 108$, NSCLC stage I–II $N = 176$, breast stage I–III $N = 490$). Complications within 3 months of diagnosis were gathered from the medical records. Complications registered were minor infections (e.g. wound infections, wound dehiscence, urinary tract infections), major infections (e.g. abscess, peritonitis, anastomotic leakage), pulmonary complications (e.g. pneumonia), haemorrhage (requiring blood transfusion or reoperation), thrombo-embolic events, cardiac failure (e.g. cardiac insufficiency), kidney failure, stoma problems (e.g.

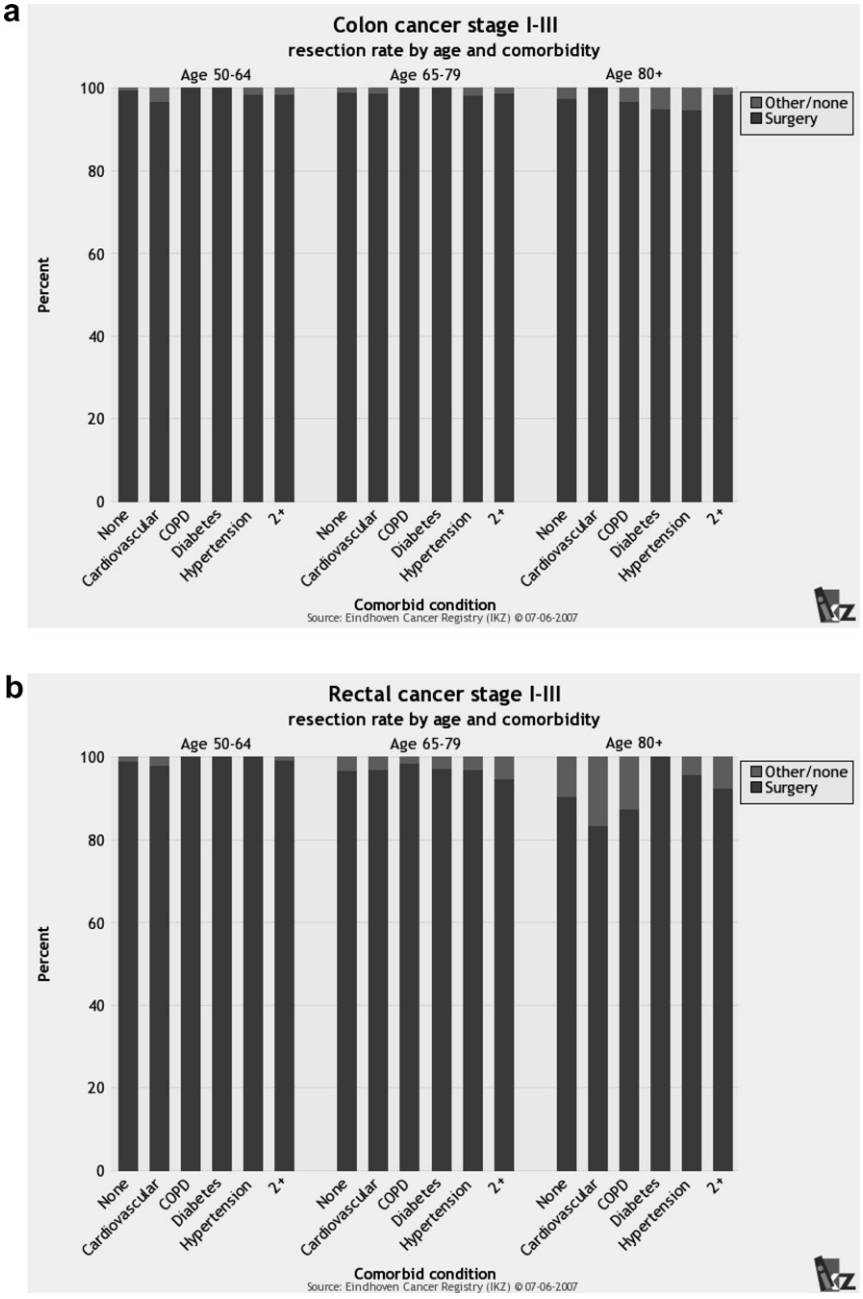
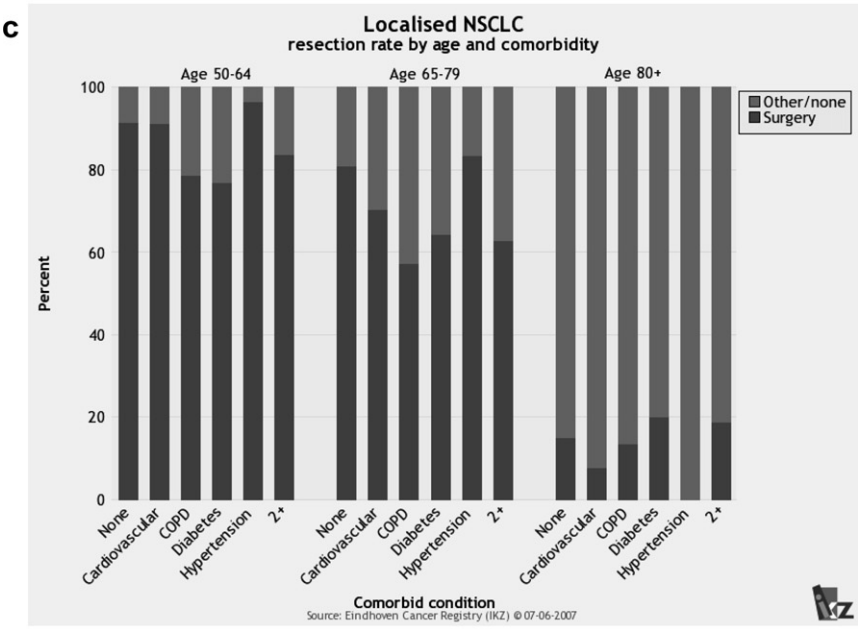


Fig. 1 – Resection rate according to age and type of comorbidity. (a) Colon cancer (stage I–III). (b) Rectal cancer (stage I–III). (c) NSCLC (stage I–II). (d) Breast cancer (stage I–III).



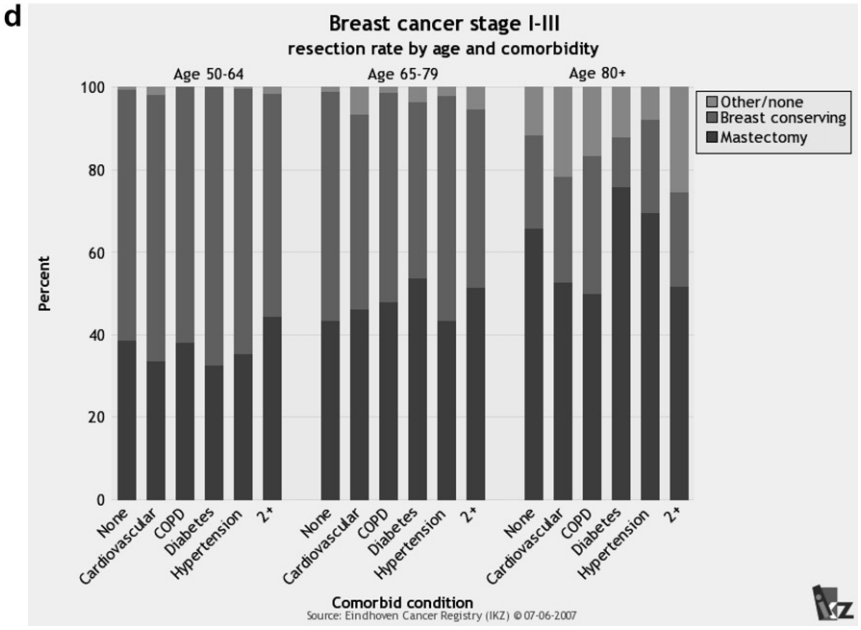


Fig. 1 (*continued*)

stomal necrosis, only for colorectal cancer) and other complications. Also death due to complications was recorded, judged from the information in the medical record as to whether the patient's death could be directly linked to a preceding complication.

Follow-up was completed up to 1 January 2006. In addition to passive follow-up via the hospitals, this information was also obtained from the municipality administration database that collects data on all deceased and emigrated persons via the civil municipal registries.

Differences in the proportion of patients undergoing surgery according to age and comorbidity were tested by means of a two-sided χ^2 test.

For resected patients, the association between comorbidity and postoperative complications was evaluated in a logistic regression model. First, a model including age, gender, stage, histology (only for NSCLC) and presence of comorbidity (yes versus no) was built. The models for colon and rectal cancer also included preoperative haemoglobin level and timing of surgery (elective or emergency), and the model for NSCLC also included type of surgery (pneumonectomy versus other surgery). Then the model was run again with the presence of comorbidity replaced by the presence of each separate comorbid condition (no comorbidity as a reference).

Survival time was defined as the time from diagnosis to death (all causes) or the end of the study. The independent

prognostic effect of the number of comorbid conditions was estimated with a multivariable Cox regression model. The hazard rates for death were adjusted for age, gender, histology (only for NSCLC) and stage. With respect to comorbidity, also the prognostic effects of the specific diseases were evaluated. For the latter, a separate model was built for each of the most common concomitant diseases (cardiovascular diseases, COPD, diabetes and hypertension). The SAS computer package (version 8.2) was used for all statistical analyses (SAS Institute Inc., Cary, North Carolina, USA, 1999).

3. Results

3.1. Surgery

Table 1 shows the general characteristics and resection rates of the patients.

Almost all patients with stage I–III colon cancer and stage I–III rectal cancer underwent surgery regardless of age or comorbidity (Fig. 1a and b). The proportion of patients with stage I–II NSCLC who underwent surgery was only 15% of those aged 80 or older versus 88% of age group 50–64 and 67% of those aged

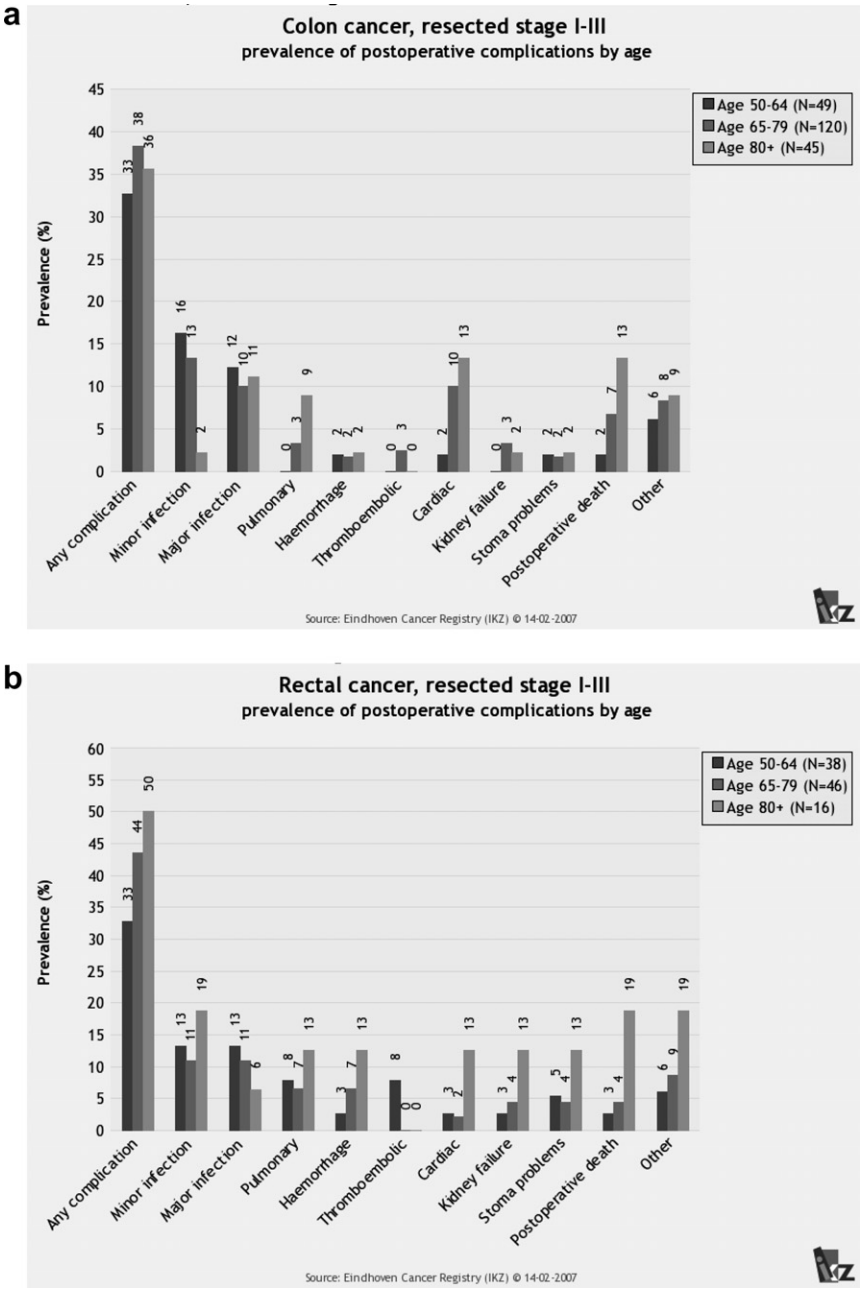
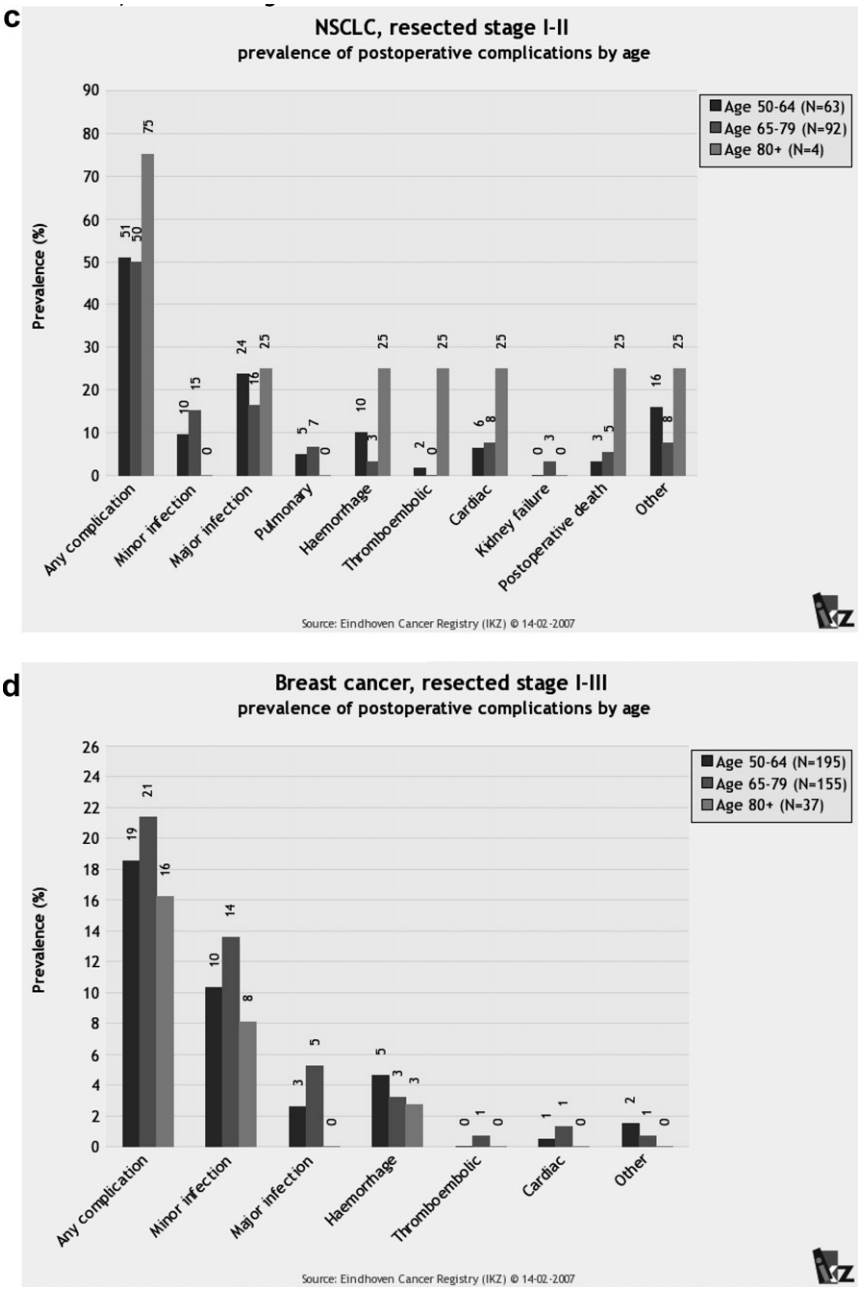


Fig. 2 – Age-specific prevalence of postoperative complications during the first 3 months after diagnosis (1995–1999). (a) Colon cancer, resected stage I–III. (b) Rectal cancer, resected stage I–III. (c) NSCLC, resected stage I–II. (d) Breast cancer, resected stage I–III.



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65–79 ($P < 0.01$) (Fig. 1c). Among patients up to 80 years, the resection rate was significantly lower when COPD, cardiovascular diseases or diabetes were present or in case of 2 or more comorbid conditions. Among patients with stage I–III breast cancer younger than 80 years, 99% underwent surgery, compared with only 81% of those aged 80 or older ($P < 0.01$, Fig. 1d). Among those undergoing surgery, the application of breast conserving surgery decreased from 60% of those aged 50–64 years to 23% of those aged 80 or older ($P < 0.01$). For those aged 65 years or older, the resection rate appeared to be lower when comorbidity was present, especially cardiovascular diseases or diabetes. Axillary dissection for those undergoing breast conserving surgery also decreased in the presence of comorbidity, as did adjuvant radiotherapy (results not shown).

3.2. *Postoperative morbidity and mortality*

Thirty-five percent of resected stage I–III colon cancer patients and 44% of resected stage I–III rectal cancer patients suffered from any complication within 3 months of diagnosis (Fig. 2a and b). The most frequent complications were minor infections (11% for colon and 13% for rectum), major infections (10% for colon and 11% for rectum) and cardiac failure (9% for colon and 4% for rectum). Among colon cancer patients elderly suffered more often from pulmonary complications than younger patients ($P = 0.07$), whereas among rectal cancer patients postoperative death occurred more often among elderly than younger patients ($P = 0.06$). The risk of developing a postoperative complication was significantly

higher for patients with emergency surgery compared to elective surgery (72% versus 34% for colon cancer, $P < 0.01$). Colon cancer patients undergoing emergency surgery suffered more often from pulmonary, cardiac, kidney and stoma complications, and postoperative death. Cardiac complications occurred more often among colon cancer patients with COPD or cardiovascular disease compared to those without comorbidity (14%). In logistic regression analysis including age, comorbidity, emergency surgery and haemoglobin level, the risk of developing any postoperative complication among colon cancer patients was significantly higher for those undergoing emergency surgery (OR = 3.63, 95% CI 1.36–9.71). Two to three percent of patients with colon or rectal cancer aged 50–64 and 13–19% of those aged 80 or older died due to complications. Nine of 21 patients who died postoperatively suffered from cardiovascular diseases and/or COPD before surgery, 6 underwent emergency surgery (6 of 15 among colon cancer), and 12 of 21 patients suffered from major infection and/or cardiac complication after surgery.

Fifty percent of patients with stage I–II NSCLC younger than 80 who underwent surgery suffered from one or more complications within 3 months of diagnosis compared to 75% ($N = 3$!) of elderly (Fig. 2c). The most frequent postoperative complications were major infections (19%) and minor infections (13%). Major infections occurred more often among patients with diabetes compared to those without comorbidity (38%). In logistic regression analysis, the risk of developing any postoperative complication was not significantly related to any of the comorbid conditions, age or pneumonectomy (results not shown). Postoperative death occurred in 25% of patients aged 80 or older ($N = 3$) compared to 3–5% of those younger than 80 ($P < 0.01$). Three of nine patients who died postoperatively suffered from COPD or cardiovascular disease before surgery, four patients had a major infection, one patient had a pulmonary complication, one had a cardiac complication, one had a combination of a major infection and kidney failure, and one had a combination of haemorrhage, thrombo-embolic complication and cardiac complication.

The proportion of breast cancer patients with complications after surgery was 19% for age group 50–64, 21% for age group 65–79 and 16% for age group 80+ (no significant difference, Fig. 2d). Minor infection (10%) was the most common complication. In logistic regression analysis, however, the risk of developing any postoperative complication was not significantly related to any of the comorbid conditions and neither to age or type of surgery (results not shown).

3.3. *Overall survival*

In multivariable survival analysis among patients with resected tumours, the risk of death increased with increasing age, even after adjustment for gender, stage, histology and presence of comorbidity. Comorbidity also had an independent prognostic effect for patients with colon cancer, rectal

Table 2 – Multivariable analysis of overall survival for resected patients aged 65 years or older with colon, rectal, NSCLC and breast cancer

	Stage I–III colon ($N = 2794$)		Stage I–III rectum ($N = 1247$)		Stage I–II NSCLC ($N = 754$)		Stage I–III breast ($N = 3141$)	
	HR[a]	95% CI	HR[a]	95% CI	HR[a]	95% CI	HR[a]	95% CI
Age								
50–64[b]	1		1		1		1	
65–79	1.66	1.50–1.84	1.67	1.47–1.90	1.47	1.31–1.64	1.69	1.54–1.89
80+	3.39	3.02–3.81	3.06	2.59–3.60	2.38	1.61–3.52	4.01	3.58–4.48
Gender								
Male[b]	1		1		1			
Female	0.83	0.77–0.90	0.86	0.77–0.95	0.67	0.58–0.78		
Histology								
Squamous cell[b]					1			
Adenocarcinoma					1.06	0.94–1.20		
Large cell undiff.					1.30	1.09–1.56		
Stage								
I[b]	1		1				1	
II	1.53	1.36–1.71	1.55	1.36–1.78			2.03	1.86–2.23
III	2.84	2.53–3.19	2.48	2.17–2.83			3.27	2.90–3.69
Comorbidity								
None[b]	1				1		1	
One condition:	1.42	1.29–1.56	1.33	1.17–1.51	1.10	0.95–1.26	1.20	1.09–1.32
Cardiovascular	1.55	1.35–1.79	1.37	1.09–1.72	1.11	0.90–1.36	1.28	1.05–1.56
COPD	1.51	1.24–1.85	1.68	1.31–2.15	0.98	0.80–1.19	1.42	1.11–1.82
Diabetes	1.30	1.04–1.64	1.30	0.95–1.79	1.20	0.79–1.82	1.25	1.01–1.56
Hypertension	1.09	0.94–1.28	1.22	1.00–1.50	0.99	0.74–1.33	0.98	0.85–1.12
Two or more	1.76	1.60–1.93	1.79	1.57–2.05	1.29	1.12–1.48	1.89	1.71–2.08

a Hazard ratio for death.
b Reference category.

cancer and breast cancer (Table 2). Among patients with stage I–II NSCLC, only the presence of two or more comorbid conditions had an independent prognostic effect. When separate comorbid conditions were evaluated in multivariable models, cardiovascular diseases, COPD and diabetes had an independent prognostic effect among patients with colon or breast cancer (see also Fig. 3a and d). Among patients with rectal cancer, cardiovascular diseases and COPD had an independent prognostic effect (see also Fig. 3b). Among patients with stage I–II NSCLC none of the specific diseases had a significant effect (see also Fig. 3c, only age group 65–79, because there were not enough patients in age group 80+).

4. Discussion

4.1. *Surgery*

When surgery is inevitable, like in patients with colorectal cancer, higher age or the prevalence of comorbidity did not significantly affect the resection rate. Surgery is the cornerstone for cure. Its goal is also to gain immediate relief of symptoms. Treatment options that do not focus on immediate relief of symptoms were, however, less applied in the elderly: several previous studies have shown that elderly patients with stage III colon carcinoma received less adjuvant chemother-

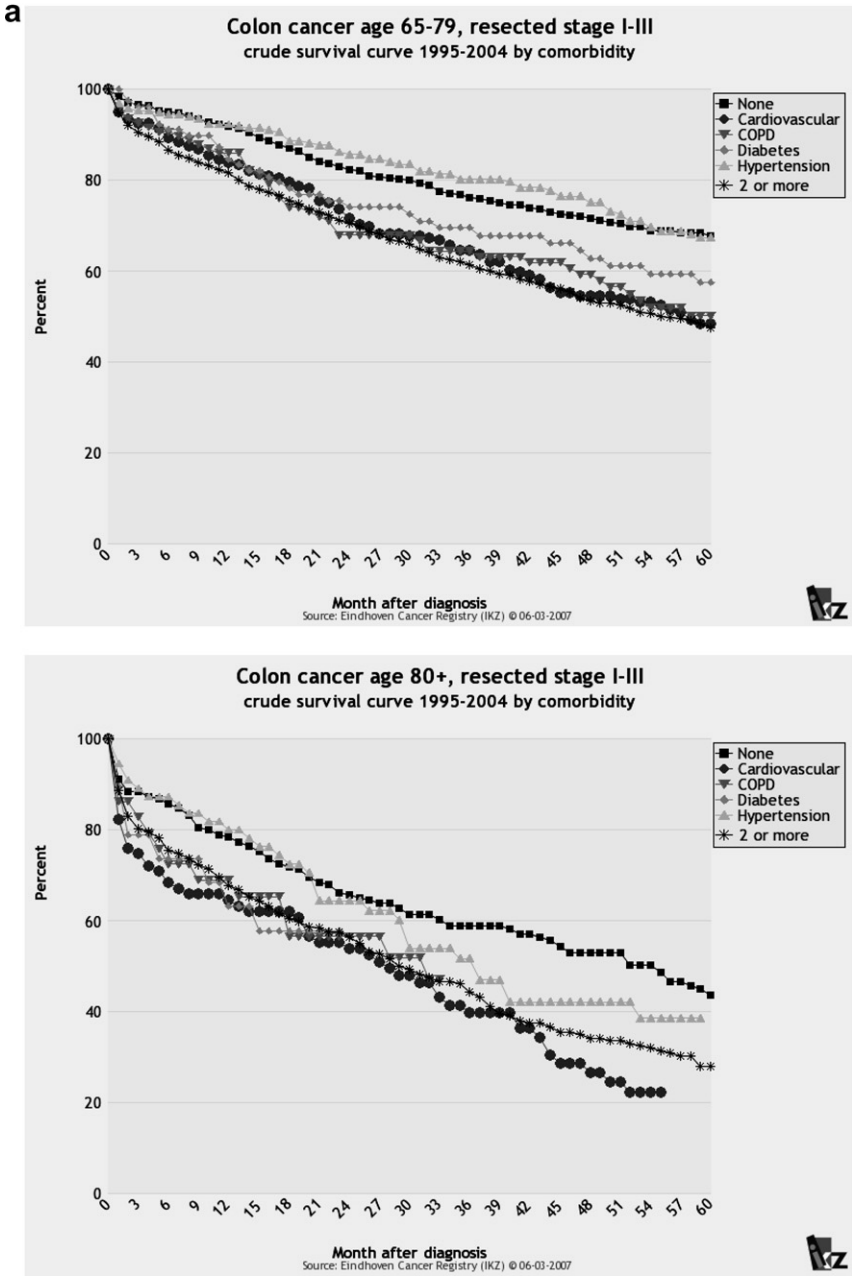
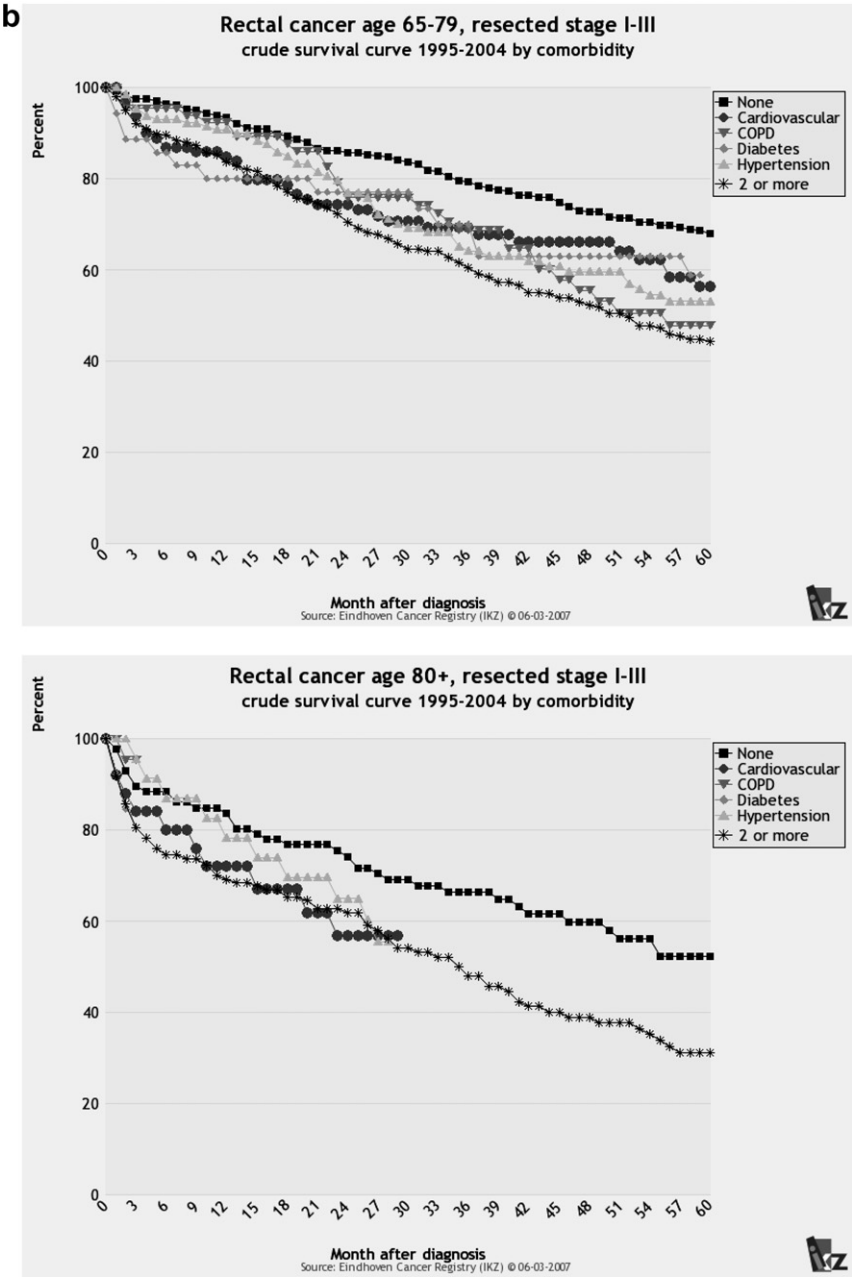


Fig. 3 – Overall survival, according to age and comorbidity. (a) Colon cancer, resected stage I–III. (b) Rectal cancer, resected stage I–III. (c) NSCLC cancer, resected stage I–II. (d) Breast cancer, resected stage I–III.



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apy and elderly patients with rectal cancer received less preoperative radiotherapy.[9–12] The influence of age on the resection rate of breast cancer was also of less importance, probably because breast surgery is a low specific risk surgery, although elderly are less likely to undergo breast conserving surgery, axillary node dissection, postoperative radiation or chemotherapy.[13–17] Despite 'undertreatment' by conventional criteria, the rates of local recurrence and distant metastasis in resected breast cancer patients in the USA were not increased in comparison with conventionally treated elderly patients.[16] In our study, breast cancer patients also underwent less surgery when cardiovascular diseases or diabetes were present. Previous studies from the USA, the Netherlands and Switzerland have shown that comorbidity also had an independent influence on receiving postoperative radiotherapy.[2,14,15,17–21]

Older patients with stage I–II NSCLC (with serious comorbidity) more often received radiotherapy instead of surgery. The same was found in previous British, American, Japanese and Dutch studies.[20,22–27] Surgical mortality for lung cancer patients increased markedly with age and was especially high for pneumonectomy.[6,28–30] In our study, the resection rate was also lower in case of comorbidity (especially COPD), probably because of the expected higher incidence of postoperative complications and mortality.[5,6,25,31,32]

4.2. *Postoperative morbidity and mortality*

Table 3 gives an overview of the literature concerning influence of comorbidity on postoperative morbidity/mortality. Previous studies have shown that perioperative risk is not

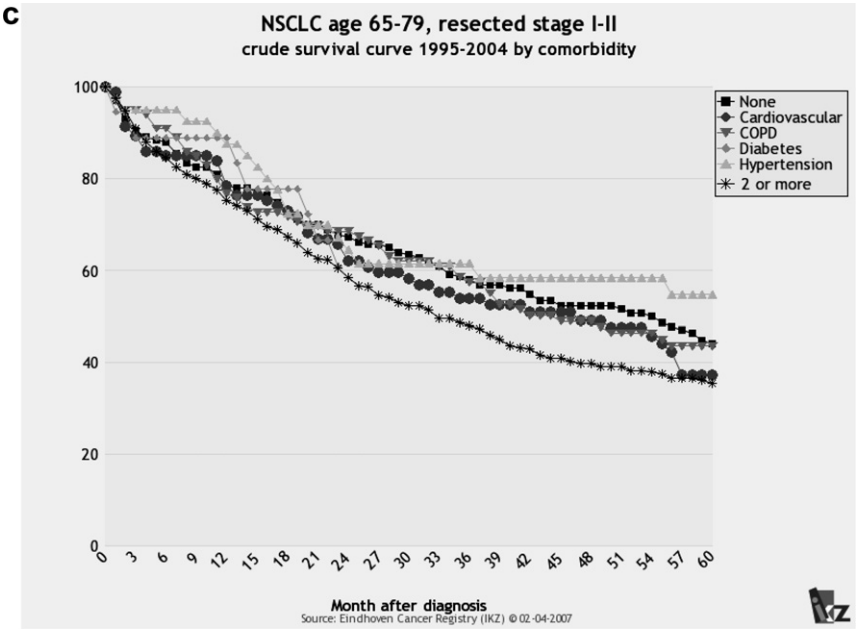

Fig. 3 (*continued*)

really different in healthy elderly and younger patients undergoing surgery for breast cancer,[33,34] suggesting that age by itself is not the key determinant of perioperative risk. The fact that elderly breast cancer patients and those with comorbidity did not have more postoperative complications than younger patients might be explained by the fact that breast surgery is low risk surgery, and also by (appropriate) selection for surgery.[34] Generally speaking, surgery is often inevitable in colorectal cancer patients. However, there is some difference between rectal cancer and colon cancer patients. In colon cancer patients obstructive tumours can often be resected or successfully bypassed, thus preserving bowel continuity even in a palliative setting. In rectal cancer patients, resection in advanced cancer stages is a major procedure, and especially in the palliative setting radiotherapy combined with stenting may be considered. However, if unresected, rectal cancer patients will often end with a diverting stoma to alleviate the symptoms of the pelvic tumour. In our study we indeed found a higher risk of postoperative complications among those who underwent emergency surgery. Special pre-, peri- and postoperative attention for patients with deep vein thrombosis at cancer diagnosis or following cancer diagnosis is warranted, because of the significant higher postoperative complication rate and poorer survival that was found in several studies.[35–38] The number of patients with deep vein thrombosis at cancer diagnosis in our study was too small to draw conclusions. In a recent study with data from the Memorial Sloan–Kettering Cancer Center, preoperative major comorbidity (heart, lung, liver, kidney disease and/or diabetes) was the only clinicopathologic factor associated with postoperative complications in patients with rectal cancer.[39] The presence of COPD and cardiovascular diseases has also been shown to be associated with postoperative morbidity in colorectal cancer.[37,40,41] In our study, postoperative mortality among colorectal cancer patients was associated with COPD or cardiovascular comorbidity, emergency surgery or major postoperative infections or postoperative cardiac morbidity. In previous studies, postoperative mortality among colorectal cancer patients was related with comorbidity in general, neurological or cerebrovascular comorbidity and postoperative complications.[37,40–44]

Among patients with NSCLC, vascular diseases, insulin-dependent diabetes, COPD, hemiplegia and pulmonary functions were predictive for postoperative complications.[6,31,45–48] In our study, 3 out of 9 NSCLC patients who died postoperatively suffered from COPD or cardiovascular disease before surgery. In previous studies postoperative mortality was higher among elderly, those undergoing pneumonectomy, preoperative FEV1 (Forced Expiratory Volume) <60%, % of predicted VO_{2max} and patients with COPD and/or cardiovascular disease.[6,27,28,31,32,45–50] Others did not find a significant effect of comorbidity on postoperative mortality.[51,52]

4.3. *Survival*

Table 4 gives an overview of the literature concerning influence of comorbidity on survival. For patients with colon, rectal or breast cancer, comorbidity had an independent prognostic effect.[10,14,15,21,34,36,53–56] This negative influence of comorbidity on survival of cancer might be due to several mechanisms: the increased risk of death due to the comorbid condition itself, neglect of treatment of the comorbid condition, more contra-indications for anti-cancer treatment, or a higher rate of treatment-related complications. In several previous studies the adverse effects of comorbidity on survival appeared to be independent of cancer treatment, so less aggressive treatment could not (fully) account for the observed differences in survival between patients with and without comorbidity.[10,14,15,21,24,34,36,53,56] In previous studies, the number of postoperative complications was also found to be an independent prognostic factor.[23,36,38,39,43,56–59]

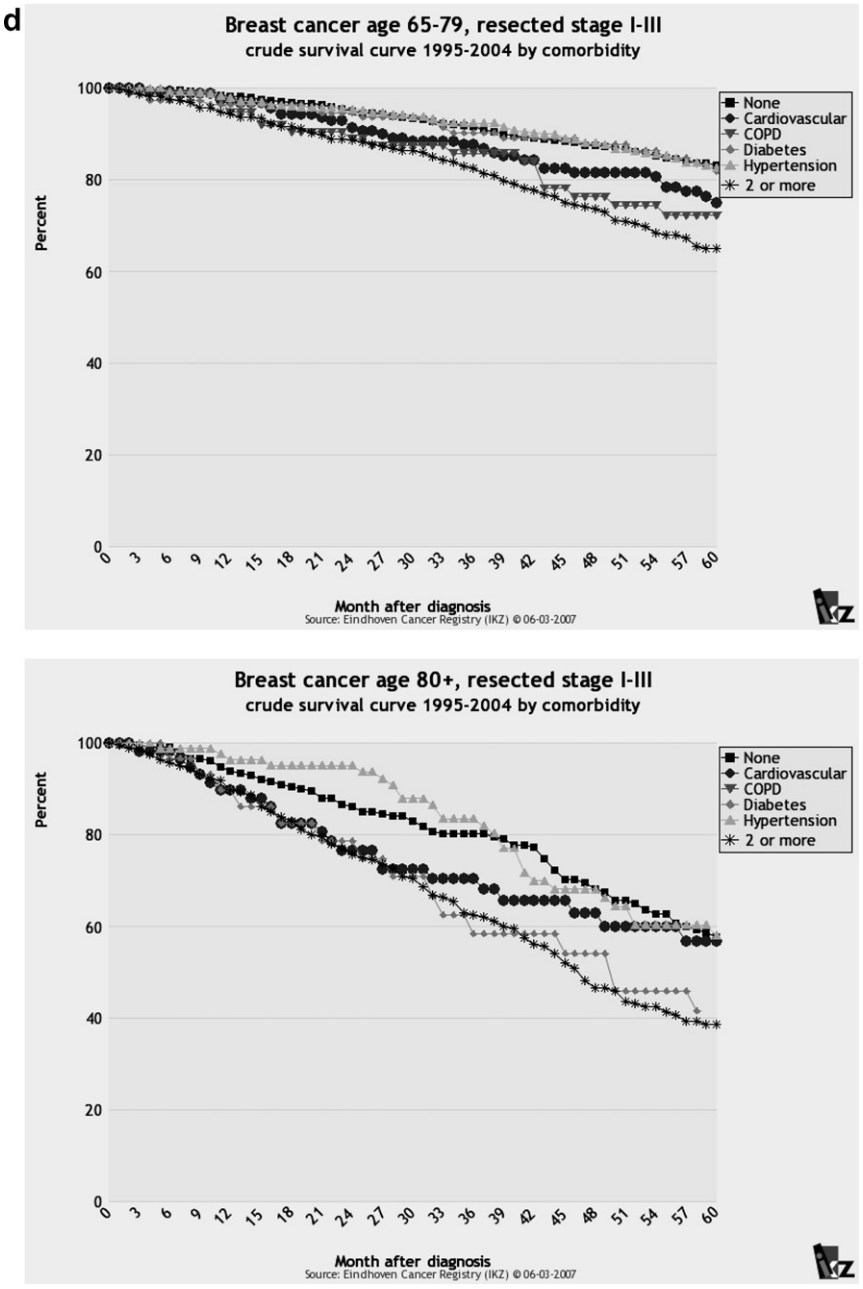

Fig. 3 (*continued*)

Among patients with lung cancer in our study, only the presence of 2 or more comorbid conditions had an independent prognostic effect.[24] In other studies also one comorbid condition had a prognostic effect.[27,47,49,52,54,55,60–62] In some previous studies other scales for measuring comorbidity were used: the Kaplan–Feinstein Index[61] and the Cumulative Illness Rating Scale-Geriatric (CIRS-G).[63] In one of the studies, comorbidity affected overall survival in surgically resected stage I NSCLC patients, when comorbidity was rated according to CIRS-G, but not according to the Charlson scale.[60] In another American study comorbidity count and the Charlson index were significant predictors for lung cancer survival, but only explained 2.5% and 2.0% of the survival variation, respectively.[62] Probably the influence of comorbidity on survival is of less importance in the case of a lethal disease such as lung cancer. Possibly many of these patients die of lung cancer, before they become at risk of dying from the comorbid condition. This was confirmed in two American studies, in which the prognostic effect of comorbidity was found to be smallest for tumours with a poor prognosis.[54,55] Especially reduced pulmonary function and cardiovascular diseases seemed to have an independent effect on survival of lung cancer.[27,49,51]

Although the proportion of postoperative morbidity and mortality was significantly higher among elderly with colorectal cancer or stage I–II NSCLC (especially those with reduced pulmonary function or cardiovascular comorbidity), current medical practice is that elderly patients undergo

Table 3 – Overview of the literature concerning influence of comorbidity on postoperative morbidity/mortality

Tumour	Age	Year of diagnosis	Reference	Influence of comorbidity on	
				Postoperative morbidity	Postoperative mortality
Colon	40+	1995–1999	37	COPD: more pneumonia or haemorrhage[b] Deep vein thrombosis: more infections, pneumonia or thrombosis[b]	Comorbidity: higher risk of dying[b]
		1993–1995, 1997–1999	36	3+ comorbidities associated with venous thromboembolism: OR = 2.0[a]	
		2002	41	Related with neurological (OR = 1.6) and cardiovascular (OR = 1.7) comorbidity[a]	Related with neurological comorbidity[a]
	All	1991–1995	40	COPD, pneumonia or CVA: more 30-day morbidity (OR = 1.3, 2.5, 1.4 resp.)[a]	CVA: more 30-day mortality (OR = 1.9)[a]
Rectal	40+	1995–1999	37	COPD: more postoperative morbidity[b]	Comorbidity: higher risk of dying[b]
		1993–1995, 1997–1999	36	3+ comorbidities associated with venous thromboembolism: OR = 2.0[a]	
		2002	41	Related with neurological and cardiovascular comorbidity[a]	Related with neurological comorbidity[a]
	70+	1995–2001	56	Comorbidity: OR = 2.3[a]	
	25–90	1988–2002	39	Comorbidity: more morbidity ($P = 0.02$)[b]	
NSCLC	70+	1993–1998	32		Related with cardiac and respiratory diseases[b]
	61–66	1990–2004	6	FEV1 < 60%: OR = 2.7[a]	FEV1 < 60%: OR = 1.9[a] 3+ cardiovasc risk factors: OR = 2.4[a]
		1990–1997	49		Related with cardiovasc comorbidity[b]
	67+	1999	27		COPD and/or cardiovascular comorbidity: higher 2-month mortality[b]
	All	1993–1994	45	Vascular disease: OR = 2.2[a] Insulin-dependent diabetes: OR = 2.8[a] Respiratory disease: OR = 1.5[a]	Vascular disease: OR = 2.8[a]
	All	1991–1995	46	COPD: OR = 1.3[a]; hemiplegia: OR = 2.6[a]	
Stage I	80+	1980–2002	51		NS[a]
Stage I		1994–1999	52		NS[a]
Resected	All		31	Related with % of predictive VO_{2max}	Related with % of predictive VO_{2max}
Resected	All	1992–1997	47	COPD: more postoperative morbidity[b]	COPD: higher postoperative mortality rate[b]
Resected	All	2004–2005	48	Cardio-respiratory morbidity related with FEV1	
Breast	40+	1995–1999	34	NS[b]	

NS, not significant.
a Multivariable analysis.
b Univariable analysis.

surgery if they are fit enough. There are three future ways to achieve better outcomes. First, selection for surgery will improve because of new and better staging techniques (e.g. MRI/PET-scanning). Preoperative selection in elderly is essential, considering the adagium 'do not harm'. Secondly, preoperative selection and interventions should focus on comorbidity and general functioning of especially older patient groups. Comprehensive geriatric assessment (CGA)[64,65] and a proper screening tool are recommended. Thirdly, an integrated care programme consisting of combined surgical and medical specialists can achieve less complications and deaths in elderly surgical patients.[66,67]

Table 4 – Overview of the literature concerning influence of comorbidity on survival

Tumour	Age	Year of diagnosis	Reference	Influence of comorbidity on survival
Colon		1993–1995, 1997–1999	36	Postoperative venous thromboembolism: HR = 1.8[a] Comorbidity: HR = 1.2–2.1[a]
	50+	1995–2001	10	HR = 1.2–1.4[a]
	55+	1992	53	HR = 1.3–2.5[a]
	All	1995–2001	54	HR = 1.4–1.7[a]
Localised	All	1991–1995	38	Venous thromboembolism: HR = 3.2[a]
Regional	All	1991–1995	38	Venous thromboembolism: HR = 2.2[a]
Localised	All	1995–2001	55	HR = 2.5[a]
Rectal		1993–1995, 1997–1999	36	Postoperative venous thromboembolism: HR = 1.8[a]; comorbidity: HR = 1.2–2.1[a]
	70+	1995–2001	56	Comorbidity: OR = 1.7[a]
	50+	1995–2001	10	HR = 1.3–1.6[a]
	All	1995–2001	54	HR = 1.4–1.7[a]
Localised	All	1991–1995	38	Venous thromboembolism: HR = 3.2[a]
Regional	All	1991–1995	38	Venous thromboembolism: HR = 2.2[a]
NSCLC		1990–1997	49	Five-year survival 1.5× higher in group without cardiovascular comorbidity[a]
	67+	1999	27	COPD: HR = 1.1[a] Cardiovascular: HR = 1.4[a]
Stage I	80+	1980–2002	51	FEV < 1.5 L: HR = 2.5[a]
Stage I	46–83	1990–1998	60	CIRS-G(4): HR = 3.4[a]
Stage I + II	All	1995–1999	24	NS[a]
Stage I		1994–1999	52	HR = 1.9–2.2[a]
		1995–1998	62	HR = 1.2–4.5[a]
	All	1995–2001	54	HR = 1.2–1.5[a]
Resected	All	1992–1997	47	COPD: poorer prognosis[b]
Stage I + II	All	1995–2001	55	HR = 1.8[a]
Localised	All	1991–1995	38	Venous thromboembolism: HR = 3.1[a]
Breast	40+	1995–1999	34	High impact comorbidity: OR = 2.9[a]
	All	1995–2001	15	HR = 1.3–2.3[a]
	All	1995–2001	54	HR = 1.8–2.0[a]
	70+	1992–1999	21	HR = 1.5–2.1[a]
	80+	1989–1999	14	Acute or subacute comorbidity: poorer overall mortality
Localised	All	1991–1995	38	Venous thromboembolism: HR = 6.6[a]
Regional	All	1991–1995	38	Venous thromboembolism: HR = 2.4[a]
Localised	All	1995–2001	55	HR = 2.9[a]

NS, not significant; CIRS-G, Cumulative Illness Rating Scale.
a Multivariable analysis.
b Univariable analysis.

5. Conclusions

Our study emphasises that comorbidity primarily has an impact on overall survival and less on postoperative complications, although high rates of postoperative complications remain. Comorbidity also leads to withholding surgical interventions if surgical therapy is commonly recognised as 'high risk' (e.g. stage I–II NSCLC) or if alternative non-surgical treatment is available (e.g. stage I–III breast cancer). Previous studies have shown that operative risk is especially high among colorectal cancer patients with reduced pulmonary function, cardiovascular diseases or neurological comorbidity or those undergoing emergency surgery, and NSCLC patients with COPD or cardiovascular diseases. Among patients with colorectal or breast cancer, comorbidity in general, cardiovascular diseases, COPD, diabetes (only colon and breast cancer) and venous thromboembolism had a negative effect on overall survival, whereas the effect of comorbidity on survival of stage I–II NSCLC was less clear. Since elderly patients with comorbidity are often excluded from clinical trials, most results were drawn from non-randomised studies, in which preoperative selection has played a major role. This indicates the need for prospective studies for refining selection criteria for surgery in elderly cancer patients in order to prevent complications where possible and to anticipate complications. Future studies should also include quality of life, because for elderly quality of life is often more important than the number of life years gained.

Take home messages

1. Patients with comorbidity often have a poorer survival
2. Anticipate postoperative complications in case of:
   (a) (Elderly) colorectal cancer patients with reduced pulmonary function, cardiovascular diseases or neurological comorbidity.
   (b) (Elderly) NSCLC patients with reduced pulmonary function or cardiovascular diseases.

3. Prospective studies are needed for evaluating:
   (a) Screening tools or selection criteria for surgery in elderly or those with comorbidity.
   (b) Complications and recurrence rates in elderly cancer patients.
   (c) Quality of life in elderly cancer patients.

Conflict of interest statement

None declared.

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