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Pneumococcal vaccination in splenectomised cancer patients

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Abstract

Although pneumococcal vaccination has been recommended in splenectomised patients for more than 30 years, its use remains unsatisfactory. We conducted two consecutive retrospective assessments to determine the rate of pneumococcal vaccination among splenectomised cancer patients at a single institution. We found that 75% (82 of 115) of splenectomised cancer patients had received at least one documented pneumococcal vaccination as compared to only 59.7% of patients identified in a previous assessment conducted 1997. 20% (22 of 115) of the patients had not been vaccinated at all. Splenectomy was performed in 54% because of Hodgkin lymphoma. The pneumococcal vaccination coverage in this subgroup has risen from 40% in the previous assessment (1997) to 93% in the current survey. In conclusion, patients splenectomised at a young age because of Hodgkin lymphoma are the key group at risk for insufficient pneumococcal vaccination. Repeated assessments of the pneumococcal vaccination status increased the rate of vaccination.

Keywords: Vaccination; Pneumococcal; Splenectomy; Cancer; Hodgkin lymphoma

1. Introduction

Patients who are asplenic or who have functional hyposplenism are at lifelong risk for a variety of serious infections especially from encapsulated bacterial organisms [1,2]. Life threatening infections occur at an estimated incidence of 0.23–0.42% per year, with a lifetime risk of 5% [2–5]. Previous reports have emphasised that the risk of overwhelming postsplenectomy infections (OPSI) is highest within the first few years after surgery. However, a recent study demonstrated that an increased risk of severe sepsis persists lifelong with a cumulative death rate of about 50% [1].

The most common infectious agent causing fulminate sepsis and OPSI in splenectomised patients is *Streptococcus pneumoniae* accounting for up to 90% of isolates from blood cultures. *Haemophilus influenzae* type b (Hib) was the second most frequent organism at the time when Hib conjugate vaccines were not available. Other species include *Streptococcus* group B, *Staphylococcus aureus*, *Salmonella* species, *Escherichia coli* and other coliforms, *Capnocytophaga canimorsus*, and rarely *Pseudomonas aeruginosa* [2].

Vaccination against pneumococcal infections in patients undergoing splenectomy has been recommended since the 1970s. Two vaccines against *S. pneumoniae* are currently available: a non-conjugated polysaccharide vaccine including 23 capsular serotypes, and a tetanus-conjugate heptavalent vaccine [4,6]. Current guidelines indicate that one vaccination prior to splenectomy and a booster injection 5 years later are recommended for patients younger than 65 years [6–9]. Pneumococcal vaccine is considered a cost-effective intervention with cost savings per life years ranging from 6500 to 28 000 US dollars [10]. However, pneumococcal vaccine is not

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100% effective and other organisms may also cause OPSI. Thus, patient information at the time of splenectomy is crucial. Deficiencies in both patient education and vaccination policies have been reported [1,4].

In a previous study at our institution conducted in 1997, we found pneumococcal vaccination in 59.6% of our splenectomised cancer patients [11]. Since this rate was considered inadequate, we have initiated a second assessment that is reported here.

2. Patients and methods

Cancer patients who had undergone splenectomy between 1970 and 2002 at our institution were identified using electronic and paper databases at our hospital tumour registry. In addition, clinical reports of all hospital patients were screened for the term "splenectomy". Moreover, all patients treated in Hodgkin lymphoma trials during this period were specifically analysed.

Starting in January 2003, a detailed questionnaire covering vaccination and information status was mailed to all patients identified. Patients were asked to return a copy of their vaccination certificate. In addition, each patient's general practitioner received the current guidelines of the Centres for Disease Control (CDC) [6,13,14] on pneumococcal vaccination together with a copy of the letter sent to his/her patient. Unresponsive patients were reminded with a second letter. The remaining non-responders were traced through direct contact of their general practitioners.

Patients who had not been vaccinated or who had an incomplete or unknown pneumococcal vaccination status received a letter recommending the vaccination. In addition, the administration of a single dose of *H. influenzae* type b and meningococcal vaccine was recommended to patients and general practitioners [2,6]. Patients were also asked to return a copy of their vaccination document signed by their general physician indicating that vaccination has been performed. In this study no assessment of anti-pneumococcal antibodies was performed, and the rate of vaccination is exclusively based on vaccination certificates.

3. Results

205 splenectomised cancer patients were identified. 115 patients, defined as 100% for the following analyses, were still alive at the time of this assessment (January 1, 2003). 55% of these patients were male and 45% female. The mean interval between splenectomy and this assessment was 12.7 years with a range from 1.1 to 32.2 years. The mean age of the patients at splenectomy was 54.2 years with a range from 28 to 85 years. The reasons for splenectomy are depicted in Table 1 with lymphoma staging procedures and gastric or oesophageal surgery being most frequent.

Table 1
Reasons for splenectomy in 115 cancer patients splenectomised between 1970 and 2002

	Patients (*n*)	%
Hodgkin lymphoma	63	58
Gastric/oesophageal cancer	15	12
Non-Hodgkin lymphoma	15	12
Pancreatic cancer	5	4
Colon cancer	5	4
Various[a]	12	10

[a] This includes: ovarian cancer (3 patients), chronic lymphatic leukaemia (3), hepatocellular carcinoma (1), acute lymphoblastic leukaemia (1), kidney cancer (1), leiomyosarcoma of the uterus (1), pseudomyxoma peritonei (1), and liposarcoma (1).

Despite considerable efforts, no information was available from 6 of 115 patients (5.5%) who were lost to follow-up. Sufficient information was available from 109 patients. 75% (82 patients) had received pneumococcal vaccination at least once prior to the current assessment, and 31% (34 patients) had received a booster vaccine after five years. In contrast, 22 (20%) patients had never received any pneumococcal vaccination. Thus, only 55% (63 of 115 patients) had pneumococcal vaccination coverage as required by current guidelines. In 5 (4.5%) patients, the vaccination status remained unclear because patients were unaware of their vaccination status and their vaccination certificates were not available. All patients with an insufficient or unclear vaccination status were informed, and vaccination was offered at our institution or they were referred to their general practitioners.

Analysis of the questionnaires revealed that all patients knew that they had been splenectomised. However, 31 (28.5%) patients were not aware that they were more susceptible to infections after splenectomy, and only 5 (4.5%) patients had received oral antibiotics for immediate use in case of fever. None of the patients was on long-term prophylactic antibiotic therapy.

Among the patients splenectomised because of Hodgkin lymphoma, 85% had received at least one pneumococcal vaccination. The mean age of these patients at the time of this assessment was 49.8 years (range from 32 to 71 years), and the splenectomy had been performed on average 18.5 years ago with a range from 9 to 31 years. In the patients splenectomised for reasons other than Hodgkin lymphoma, we observed that 68.5% of the patients had received at least one pneumococcal vaccination. The mean age of patients in this group was 62 years (range 27–85 years) and thus significantly higher than in the group with Hodgkin lymphoma patients. Also, the interval between splenectomy and this assessment was threefold shorter than in the Hodgkin lymphoma group (6 years with a range from 1 to 29 years).

Table 2
Reasons for splenectomy in 90 cancer patients splenectomised between 1970 and 2002

	Patients (*n*)	%
Gastric/oesophageal cancer	21	23
Pancreatic cancer	19	21
Hodgkin lymphoma	15	17
Non Hodgkin lymphoma	15	17
Various[a]	20	22

These patients died before this study was initiated (January 1, 2003), and thus they were not included in the study.
[a] This includes: colorectal cancer (8 patients), lung cancer (6), kidney cancer (2), bladder cancer (2), ovarian cancer (1), and melanoma (1).

Table 3
Reasons for death in 90 cancer patients splenectomised between 1970 and 2002, who where not included in the study because of death before initiation of this study

	Patients (*n*)	%
Tumour progression	66	73
Secondary malignancies	8	9
Others[a]	15	17
OPSI[b]	1	1

[a] Others comprised cardiac events (4 patients), accidents (2), chronic pneumopathy (2), and unknown due to loss in follow-up (7).
[b] OPSI: overwhelming postsplenectomy infection.

75 of 115 (65%) patients covered by this assessment had been splenectomised before 1996 and should therefore have been contacted in the first assessment conducted 1997. However, 46 (62%) patients were not identified in the first study. We thus ended up with only 29 patients that were included in both assessments of 1997 and 2003. Interestingly, 28 of the 29 patients identified by both assessments had been splenectomised because of Hodgkin lymphoma. The vaccination coverage of these 29 patients was only 40% as assessed in the first survey 1997, and it increased to 93% by the time of the 2003 survey.

The reasons for splenectomy of the 90 patients that were not included in the study because of death before initiation of this study are listed in Table 2. Almost half of these patients had been splenectomised because of gastric or pancreatic cancer. The causes of deaths of these 90 patients are listed in Table 3. They indicate that a high proportion of patients died because of tumour progression. Seven patients were lost to follow-up. Remarkably, one patient died of overwhelming postsplenectomy pneumococcal sepsis.

4. Discussion

Compared to our previous assessment conducted seven years ago [11], the rate of pneumococcal vaccination of splenectomised cancer patients at our institution rose from 59.7% to 75%. However, the use of pneumococcal vaccination is still insufficient in a substantial portion of splenectomised cancer patients, and only a minority of patients have in fact been vaccinated according to the current guidelines. Moreover, we have found that 28% of patients were not aware of their increased risk of infection. This result is in accordance with other reports where up to 50% of asplenic patients are unaware of their increased risk of serious infection [11,12].

We identified the subgroup of patients splenectomised because of Hodgkin lymphoma as the main group at risk for insufficient pneumococcal vaccination. Staging laparotomy and splenectomy were part of routine staging procedures in patients with Hodgkin lymphoma until an EORTC trial showed 1993 that the benefit from laparotomy staging in terms of lower relapse rate was erased by more deaths due to infections [5]. Splenectomy performed at staging laparotomy in our cohort of Hodgkin lymphoma patients dated on average about 18 years ago. With the incidence of Hodgkin lymphoma peaking around the age of 25 years, many of these patients are now long-term cancer survivors after curative treatment. In the late 1970s, disagreements in published guidelines, in manufacturers' instructions and in commonly used textbooks led to low acceptance and use of pneumococcal vaccination and could possibly explain the insufficient vaccination rate among these patients [11]. We found at our institution that two consecutive assessments, seven years apart, led to a substantial increase of pneumococcal vaccination from 40% to 93% in this specific risk group. The pneumococcal vaccination coverage of 75% in this report is higher than published by others [4,15,17,18]. Subgroup analysis revealed that the pneumococcal vaccination coverage in patients splenectomised due to Hodgkin lymphoma was 85% as compared to only 68.5% in patients splenectomised because of other malignancies. The higher rate in the Hodgkin lymphoma group may have been a result of the repeated assessment, as 46% of these patients (29 of 63 patients) were contacted in 1997 and 2003 whereas none of the patients splenectomised for other malignancies were part of the first survey in 1997.

The reasons for failure to vaccinate turned out to be complex. We observed that the rate of primary vaccination was higher in patients splenectomised in the course of a routine staging procedure – such as in Hodgkin lymphoma patients – as compared to patients which were splenectomised in the course of a surgical primary tumour therapy for solid tumours. Moreover, our study comprised only cancer patients who had received subsequent treatment at our medical oncology department. We therefore can not exclude that the vaccination rate may be different in cancer patients treated by surgery alone. Interestingly, we observed no difference in the rate of vaccination among cancer patients when fol-

low-up was performed at the hospital as compared to primary physicians.

Despite considerable efforts, we failed to contact six patients. This is of particular concern since patients splenectomised particularly at young age of Hodgkin lymphoma are at lifelong risk of fatal infections. In addition, fatal pneumococcal infections in patients with insufficient vaccination may increasingly have legal consequences for responsible physicians.

This hospital based repeated survey represents a possibility to implement adequate pneumococcal vaccination coverage. However, it requires considerable resources in terms of time and staff. Moreover, we found that it remains difficult despite sophisticated hospital databases to identify all patients at risk. Others reported experiences with setting up a register of patients with asplenia within a defined geographic area [16,17]. Such a register might allow better patient contact, it may raise awareness of the management of asplenic patients and health care professionals, and it might improve vaccination rates. In addition, a pneumococcal vaccination campaign mainly reaching general practitioners is feasible and offers another possibility to substantially increase the proportion of vaccinated patients at risk [18]. We would like to suggest that asplenic patients should receive a wallet card indicating their splenectomy status similar to patients with artificial heart valves. In addition, such patients should accordingly inform any new health care professionals including dentists of their history.

Conflict of interest statement

None declared.

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