

Increased risk of primary cancer after *Staphylococcus aureus* bacteremia. A matched cohort study

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REGION

BACKGROUND

- More than one in three persons will be affected by cancer during a lifetime.
- Cancer ranks as frequent cause of death in industrialized and developing countries.
- Up to 20 % of all cancers are believed to be associated with microbial coinfection suggesting that immunity and inflammation play a central role in cancer development.
- We hypothesized that a developing cancer may be preceded by an increased susceptibility to invasive bacterial infection.

METHODS

- Danish nationwide population-based cohort study (1992-2014) based on:
 - The Danish SAB database
 - The Civil Registration System
 - The Danish National Patient Registry
 - The National Danish Cancer Registry
- 19,088 SAB cases
- 170,551 age- and gender matched controls.
- Cancer was classified into 27 categories according to the ICD 7th edition and ICD 10th revision.
- Comorbidity was estimated by the Charlson Comorbidity index (CCI) excluding cancer categories.
- Incidence rates (IR) and ratios (IRR) were analyzed by multivariate Poisson regression.
- Cumulated Hazard curves were constructed by GG-plots.

FINDINGS

- SAB cases had 77 % increased risk of developing cancer at one year (IRR: 1.77, 95% CI: 1.56-2.02).
- Within 90 days 12 cancers were more likely for cases: Thyroid, testis, non-Hodgkin lymphoma, liver, esophagus, urinary, kidney, breast, stomach and prostate.
- 5 additional types of cancer were more frequent for cases over the first year: cervix, multiple myeloma, ovary, leukemia and pancreas.
- Cases had an increased risk for both acute and chronic leukemia within a year compared to population controls.
- The frequency of cancer was depending on type, age and sex.

CONCLUSION

- Primary incident cancer in SAB patients was increased during the first year of follow-up compared to controls.
- Breast, prostate, cervix, urinary, pancreas, ovary, leukemia, stomach, kidney, liver, esophagus, multiple myeloma, testis, thyroid and non-hodgkin lymphoma were more frequent in cases than controls.
- Age and sex are influenced the risk of developing specific types of cancer.
- Screening for these specific cancers in selected populations may allow for earlier detection.

RESULTS

Table 1. Characteristics of cases with *Staphylococcus aureus* bacteraemia and their controls in Denmark from 1992-2014

	SAB cases			Controls		
	All	No Cancer	Cancer	All	No Cancer	Cancer
	N=19,088	N=18,020	N=1068	N=170,551	N=151,530	N=19,021
Sex						
Male	11,794 (61.8%)	11,087 (61.5%)	707 (66.2%)	106,370 (62.4%)	93,720 (61.9%)	12,650 (66.5%)
Female	7294 (38.2%)	6933 (38.5%)	361 (33.8%)	64,181 (37.6%)	57,810 (38.2%)	6371 (33.5%)

Figure 1. Events of cancer cases compared to population controls.

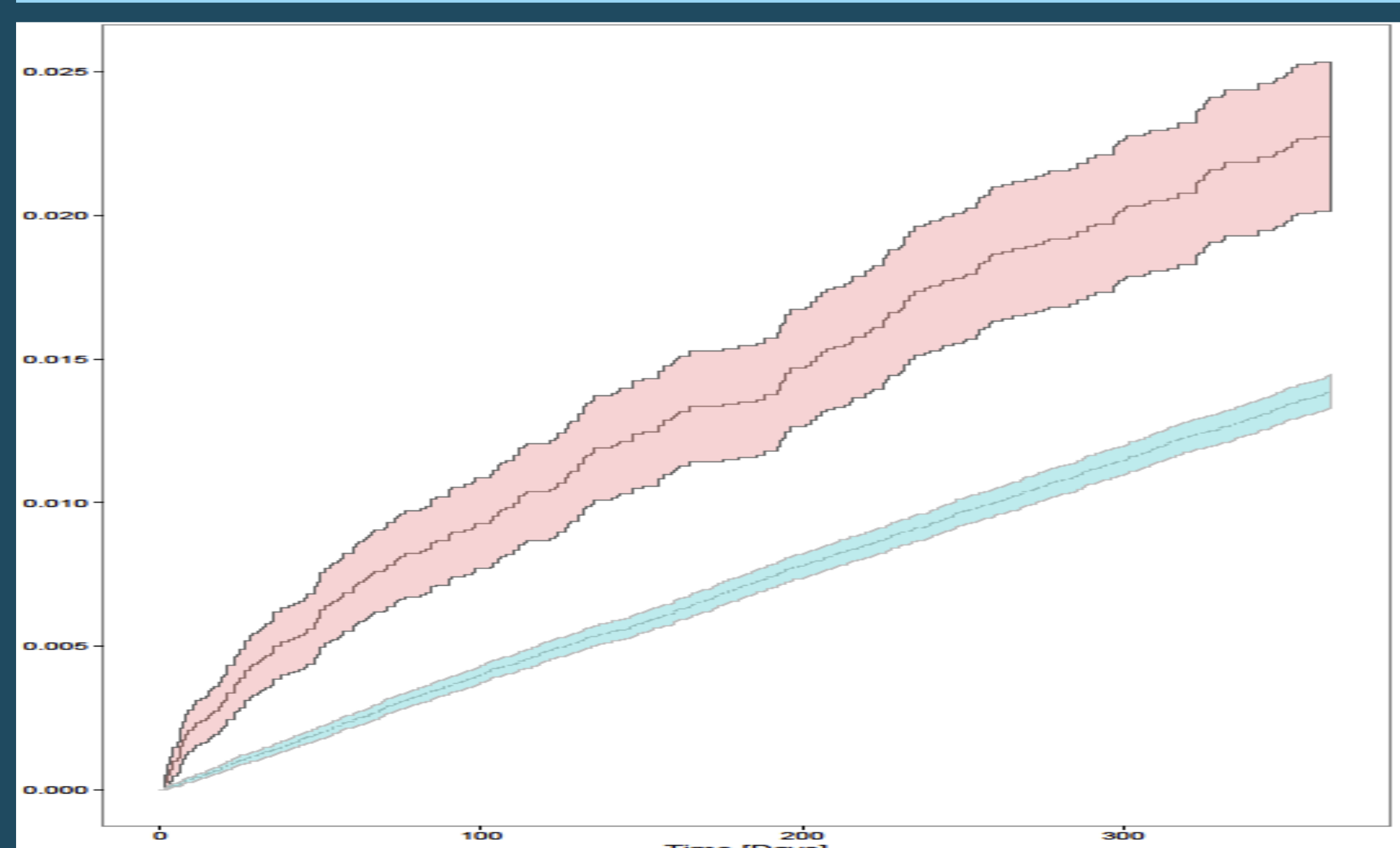


Table 2. Types of cancer and incidence rate ratios for cases and controls.

Type of cancer	Cases		Controls		Incidence rate ratio (95% CI)		
	0-90 days N=125	91-365 days N=165	0-90 days N=620	91-365 days N=1666	0-365 days	0-90 days	91-365 days
Non-Hodgkin lymphoma	6 (4.8%)	3 (1.8%)	11 (1.8%)	18 (1.1%)	5.67 (2.52-12.79)	12.40 (4.27-36.04)	2.39 (0.64-8.86)
Thyroid	1 (0.8%)	1 (0.6%)	1 (0.2%)	5 (0.3%)	9.89 (1.86-52.48)	34.69 (2.17-554.64)	5.37 (0.57-50.44)
Testis	1 (0.8%)	-	2 (0.3%)	3 (0.2%)	4.37 (0.47-40.22)	16.06 (1.44-179.65)	-
Myeloma	9 (7.2%)	8 (4.9%)	9 (1.5%)	15 (0.9%)	8.91 (4.42-17.95)	9.74 (3.42-27.75)	7.71 (2.96-20.10)
Esophageal	3 (2.4%)	2 (1.2%)	7 (1.1%)	21 (1.3%)	3.26 (1.21-8.77)	8.89 (2.12-37.20)	1.62 (0.37-7.17)
Liver	9 (7.2%)	5 (3.0%)	8 (1.3%)	27 (1.6%)	3.59 (1.76-7.32)	9.47 (3.23-27.79)	1.54 (0.53-4.50)
Kidney	6 (4.8%)	4 (2.4%)	12 (1.9%)	36 (2.2%)	2.51 (1.21-5.19)	5.17 (1.79-14.93)	1.40 (0.47-4.14)
Stomach	4 (3.2%)	3 (1.8%)	15 (2.4%)	27 (1.6%)	2.20 (0.94-5.14)	3.36 (1.03-10.97)	1.49 (0.43-5.22)
Leukemia	9 (7.2%)	10 (6.1%)	14 (2.3%)	40 (2.4%)	9.99 (4.04-12.09)	11.98 (4.91-29.23)	5.13 (2.50-10.51)
Ovary	4 (3.2%)	-	8 (1.3%)	20 (1.2%)	2.06 (0.66-6.44)	7.46 (2.02-27.48)	-
Pancreas	8 (6.4%)	8 (4.9%)	15 (2.4%)	45 (2.7%)	3.68 (2.03-6.68)	7.78 (3.04-19.90)	2.39 (1.07-5.33)
Urinary	6 (4.8%)	9 (5.5%)	18 (2.9%)	60 (3.6%)	2.80 (1.55-5.05)	6.34 (2.38-16.86)	1.94 (0.92-4.09)
Cervix	-	4 (2.4%)	-	3 (0.9%)	24.14 (4.91-118.81)	-	24.13 (4.84-120.23)
Prostate	11 (8.8%)	19 (11.5%)	69 (11.1%)	228 (13.7%)	1.38 (0.93-2.05)	2.13 (1.07-4.25)	1.22 (0.75-1.98)
Breast	8 (6.4%)	8 (4.9%)	46 (7.4%)	107 (6.4%)	1.78 (1.03-3.09)	3.44 (1.56-7.59)	1.03 (0.48-2.24)
Colon	10 (8.0%)	7 (4.2%)	82 (13.2%)	212 (12.7%)	0.72 (0.43-1.19)	1.23 (0.61-2.48)	0.45 (0.21-0.97)
Other	4 (3.2%)	6 (3.6%)	8 (1.3%)	18 (1.1%)	4.92 (2.22-10.91)	7.23 (2.05-25.68)	3.84 (1.38-10.69)

Adjusted for: All variables, Testis: age, year, mCCI, Cervix: age, year, mCCI. Insignificant cancer categories are excluded from the table as well as categories with no events in one of the groups i.e. Hodgkin disease and Small intestine cancer.

Table 2.b. Types of Leukemia and incidence rate ratios for cases and controls within the first year of SAB.

	Cases 0-365 days	Controls 0-365 days	IRR 0-365 days
ALL	3 (15.8%)	2 (3.7%)	14.82 (2.34-93.82)
AML	6 (31.6%)	12 (22.2%)	9.79 (3.49-27.45)
CLL	5 (26.3%)	31 (57.4%)	3.59 (1.34-9.65)
CML	2 (10.5%)	2 (3.7%)	15.13 (1.98-115.35)
Other	3 (15.8%)	7 (13.0%)	9.05 (2.21-37.08)

Adjusted for: ALL: sex, year, mCCI, AML: all variables, CLL: all variables, CML: sex, age, mCCI, Other: all variables.

Table 4. Patients characteristics of specific types of cancer during the first year after *Staphylococcus aureus* bacteraemia.

	Types of cancer				
	Multiple Myeloma	Leukemia	Ovary cancer	Cervix cancer	Pancreas cancer
Age years	68 (IQR:59-83)	78 (IQR:69-80)	60 (IQR: 52-63)	74 (IQR:57-86)	65 (IQR:58-76)
Sex Female	58.8 %	21.1 %	-	-	37.5 %