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Early mortality attributable to PICC-lines in 4 public hospitals of Marseille from 2010 to 2016 (Revised V3)

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Abstract

Introduction: Peripherally inserted central catheters (PICC-line) are devices inserted through peripheral venous access. In our institution, this technology has been rapidly adopted by physicians in their routine practice. Bacteremia on catheters remains an important public health issue in France. However, the mortality attributable to bacteremia on PICC-line remains poorly evaluated in France and in the literature in general. We report in our study an exhaustive inventory of bacteremia on PICC-line and their 30 days mortality, over a 7 years period.

Material and methods: From January 2010 to December 2016, we retrospectively matched PICC-line registers of the radiology department, blood culture records of the microbiology laboratory and medical records from the Hospital Information Systems.

Results: The 11,334 hospital stays during which a PICC-line was inserted were included over a period of 7 years. Among them, 258 episodes of PICC-line-associated bacteremia were recorded, resulting in a prevalence of 2.27%. Hematology units: 20/324 (6.17%), oncology units: 55/1375 (4%) and hepato-gastro-enterology units: 42/1142 (3.66%) had the highest prevalence of PICC-line related bacteremia. The correlation analysis, when adjusted by exposure and year, shows that the unit profile explains 72% of the variability in the rate of bacteremia with a $P = .023$. Early bacteremia, occurring within 21 days of insertion, represented 75% of cases. The crude death ratio at 30 days, among patients PICC-line associated bacteremia was 57/11 334 (0.50%). The overall 30-day mortality of patients with PICC-line with and without bacteremia was 1369/11334 (12.07%). On day 30, mortality of patients with bacteremia associated PICC-line was 57/258 or 22.09% of cases, compared to a mortality rate of 1311/11076, or 11.83% in the control group ($P < .05$, RR 2.066 [1.54–2.75]). Kaplan–Meier survival analysis revealed a statistically significant excess mortality between patients with PICC-line associated bacteremia and PICC-line carriers without bacteremia ($P < .0007$, hazard ratio 1.89 [1307–2709]).

Conclusion: Patients with PICC-line associated bacteremia have a significant excess mortality. The implementation of a PICC-line should remain the last resort after a careful assessment of the benefit/risk ratio by a senior doctor.

Abbreviations: AP-HM = Assistance Publique-Hôpitaux de Marseille, CRBSI = catheter related blood stream infection, HGE = hepato-gastro-enterology, ICU = intensive care units, IV = intravenous, PICC-Line = peripherally inserted central catheters, RR = relative risk, USA = United States of America.

Keywords: bacteremia, central catheters with peripheral insertion, mortality, PICC-line

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1. Introduction

Peripherally inserted central catheters (PICC-line) are devices inserted through peripheral venous access, usually the brachial vein.[1] This technique was introduced more than 30 years ago in the United States, particularly in intensive care units. (ICU).[1,2] Nevertheless, PICC-lines were quickly discontinued, except in pediatric intensive care units. The reasons for discontinuation in adult medicine were a higher frequency of adverse events, such as catheter infections and thrombosis compared to conventional central venous routes.[2] PICC-lines became popular again in North America in the second half of the 1990s. In 2005, there were already 942,000 new PICC-lines inserted each year in the United States of America (USA).[3] These devices have been a real success in France for about ten years.[1,4,5] In our institution, this technology was introduced in 2004, and was quickly adopted by clinicians.[4]

Healthcare-related infections, especially catheters infections, are a major cause of morbidity and mortality worldwide. In the United States, 250,000 hospital-acquired blood stream infections per year have been reported, 23,000 of them been related to central venous catheter infection in 2009.[6] Another study conducted in the USA reported a mortality rate of 27% in catheter-associated bacteremia (all types).[7] Rosenthal et al, have also highlighted this problem in Europe, Asia and Africa with a study from 2004 to 2009, including 422 ICU in 36 different countries. They recorded 6.8 events per 1000 central venous catheters /days.[8] In 2014, blood stream infection accounted for 9.9% of care-related infections in the USA.[9] In France, this problem remains an important public health issue. In 2012, a national survey in France, reported that 5% of patient admitted in hospitals acquired infection during care, 10.1% of those were catheter associated blood stream infection. Of these catheters, 3.4% were PICC-lines.[10,11]

Mortality due to bacteremia on the PICC-line remains poorly assessed in the literature. The use of PICC-line is indicated only when the duration of intravenous (IV) treatment is greater than 6 days.[13,14] No mention has been made of the maximum duration since 2013, when some scientific societies recommend PICC-lines for IV therapies longer than 6 days, but whose duration must remain less than 3 months. Beyond this, it is recommended to set up an implantable chamber (port-à-cath).[15] Unfortunately, these guidelines are poorly known by clinicians.[12]

The insertion of PICC-lines is easy, fast and is performed by a simple ultrasound location of the brachial vein.[1,16] The cost/benefit ratio is very attractive.[17] Finally, in order to reduce the length of hospital stay,[18] PICC-lines appear to provide an opportunity to administer intravenous therapies for long periods of time, even at home.[1,4,19] Although the literature on the subject is relatively abundant, the risk of developing bacteremia is still poorly evaluated, especially outside intensive care units.[2,20] The infection rates of PICC-lines differ from one publication to another. Some studies find an infectious risk equivalent to that of the conventional central venous catheter,[21] in patients hospitalized in intensive care unit. It should be noted that in most previous major series, PICC-line infections have not always been screened separately from other types of central line catheters, resulting in a bias in risk assessment.[2,3,21] Finally, we find only few randomized studies in the literature.[17,22,23] This study will provide data on delay between insertion and bacteremia and the distribution of prevalence of catheter related blood stream infection (CRBSI) among medical and surgical ward. It aware on the overuse of PICC-line, and the poor outcomes in bacteriemic patient.

We report here an exhaustive inventory, over a period of 7 years, of bacteremia on PICC-line and their mortality at 30 days in all wards of our hospital. We determine the risk factors associated with bacteremia mortality and the epidemiology of the responsible microorganisms.

2. Material and method

2.1. Type of study

This is a retrospective monocentric cohort study based on comprehensive hospital registers. The study took place at the Assistance Publique-Hôpitaux de Marseille (AP-HM), France.

2.2. Study population

AP-HM is a university structure that includes four major hospitals accounting for 3500 beds and up to 125,000 admissions per year. The insertion of PICC-lines is carried out in 2 radiology departments, one in the northern suburb of the town (North Hospital) and one in downtown (Timone Hospital). We included all patients over 18 years of age, hospitalized in our institution, who benefited from the insertion of a PICC-line from January 1, 2010 to December 31, 2016, and for whom the event "bacteremia" was recorded in the microbiology laboratory data base (cases) or not (controls) during the same hospital stay between the insertion of the PICC-line and for a subsequent period of 30 days minimum (Fig. 1).

Patients with another device and patients admitted to a pediatric ward were not included. In addition, we did not include patients with PICC-line insertion as part of an outpatient admission as well as patients whose intra-hospital follow-up was not possible. To define bacteremia on PICC-line, we relied on the revised recommendations of the Infectious Diseases Society of America.[13,14,24,25] "A definitive diagnosis of CRBSI requires that the same organism grows from at least 1 percutaneous blood sample culture and from the catheter tip (A-I) or that 2 blood samples for culture be obtained (1 from a catheter hub and 1 from a peripheral vein) that meet CRBSI criteria for quantitative blood cultures or differential time to positivity (A-II)". Patient selection was performed from the comprehensive PICC-lines insertion register provided by the radiology department. Data from selected patients were merged with our microbiology laboratory database (recording all blood cultures and their result (s) over the same period), and with the data obtained from the Hospital Information System. All these registers are recognized by the National Commission for Information Technology and Liberties. The primary endpoint was defined as the mortality within 30 days of the PICC-line insertion. For each patient, the date of death, if any, has been completed. The criteria for secondary judgments were:

1) the bacteremia on PICC-line: as defined previously, an prevalence per year and per medical unit was sought as well as the overall prevalence and per medical unit,
2) the microbiology of bacteremia: Defined as identified micro-organisms in bacteriemic patients and finally
3) the risk factors for bacteremia and mortality.

2.3. Explanatory variables

We collected data from 11 medical/surgical specialties. For each patient, we recorded sex, age, average length of stay, average

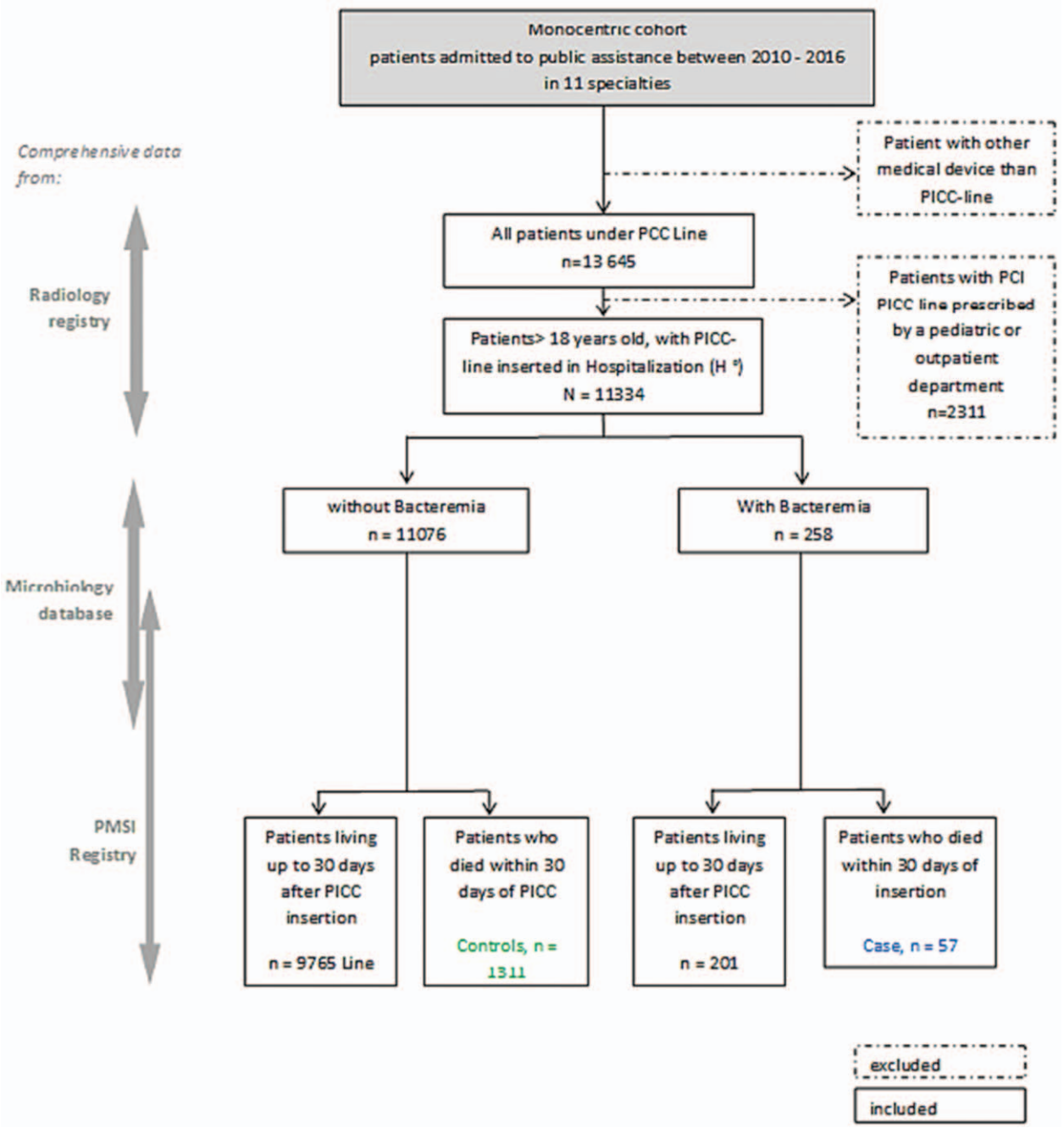

Figure 1. Study population and inclusion method (Flowchart).

length of stay before bacteremia, medical indication (parental nutrition, chemotherapy, antibiotic, saline solution), underlying conditions such as comorbidities and immunosuppression which represents a risk of infection. We also recorded the number of PICC-Line inserted each year for each specialty.[31–35] Finally, we classified all the specialties into three groups according to the literature data:[32] The group at high risk of infection (oncology, palliative care unit, hematology, hepato-gastro-enterology), the group at average risk of infection (cardiology, internal medicine / geriatrics and neurology) and the group at low risk of infection (other surgical specialties, other medical specialties and infectious diseases).

2.4. Statistical analyzes

Data from all 3 databases have been merged using the mySQL software. A descriptive analysis was performed to define the characteristics of the study population at baseline and to estimate, in each department, the prevalence of PICC-Line insertion, bacteremia, and 30-day mortality. Univariate comparative analyzes were performed to determine the risk factors (such as specialty, specialty profile) that are associated, in patients with PICC-Line, with bacteremia or mortality secondary to this bacteremia. The Chi-squared test for qualitative variables was used to measure these associations. Relative risk (RR) was calculated to estimate the strength of the association. For the

quantitative variables, a linear regression analysis made it possible to measure the correlation coefficient for the quantitative variables. An adjustment for the potential confusion variables was taken into account (such as the number of PICC-Line inserted per medical or surgical units). A Kaplan–Meier survival analysis was performed to compare mortality between PICC-line patients with bacteremia and controls. Statistical analyzes were performed using GraphPad, Prism 5.0 and SPSS 17.2 software.

This study was approved by local committee of IHU Méditerranée Infection (2016–14). All the methods were carried out in accordance to the European General Data Protection Regulation. The study is a retrospective analysis of the issue of biological data and patient registry data from the hospital's information system, which is an authorized health care database. Access to the registry has been approved by the data protection committee of our institution (AP-HM) and recorded in the European general data protection regulation registry under N° RGPD/APHM 2019–73. The study was supervised by a person who was fully aware of the confidentiality requirements.

3. Results

3.1. Characteristic of populations (Table 1)

The mean age is similar in the 2 populations, 64 years and 62, and the median ages were 66 years and 65 years respectively for the cases and the control group. The male sex ratio in cases was 0.62 compared to 0.80 in the control group ($P < .05$ RR 1.91 [1.008–1.685]). The length of stay was significantly higher in cases than in the control population; 47 days [1 day–132 days] versus 32 days [1 day -230 days] ($P < .05$). The mean hospital stay delay before bacteremia was 20 days (median of 13 days).

Table 1

Summary of key features.

	Patients with PICC-line		
	Bacteremia	Control	*P*
Average age / median (yr)	64 / 66	62 / 65	*NS*
Sex ratio	0.622	0.80	*P < .05*
Average length of hospital stays (days)	47 [1–132]	32 [1–230]	*P < .05*

NS = Not significant.

3.2. General results

Of the 13,645 PICC-lines inserted from 2010 to 2016 at the AP-HM, 11,334 were included for this study according to the criteria described above. We noted an increase in demand of 18.11% between 2010 and 2016. 2014 remains the year in which the largest number of PICC-lines were inserted in our institution, with 2,148 devices inserted (Fig. 2), an increase of 30.02% compared to 2010. The four most important prescribers for PICC-lines insertion were the "surgical specialties" 21% (out of general and digestive surgery), the cardiology department 13%, oncology 12%, and hepato-gastro-enterology 10%. The rate of bacteremia was 2.93% (39/1330) in 2010 and rose up to 3.81% (59/1547) in 2011. This was followed by a continuous decline until 2015 with 1.25% (22/1748) and then marked by a further increase in 2016 to 2.13% (24/1595) ($P = .045$) (Fig. 3). During the inclusion period, we recorded a total of 258 cases of PICC-line bacteremia, with an average prevalence of 2.27% over a period of 7 years.

3.3. Prevalence by service

The oncology, hepato-gastro-enterology (HGE) and cardiology departments had the highest prevalence of PICC-line associated bacteremia, with a prevalence of 21.31% (55/258), 16.24% (42/258) and 13.17% (24/258) respectively (Table 2). The overall prevalence in oncology was significantly higher when compared to cardiology (21.3% /13.1%) (RR 1.618 [1.094–2.392] $P = .007$), hematology (7.7%) (RR 2.750 [1.68–4.45] $P < .0001$), "other medical specialties" (8.5%) (RR 2.5 [1.573–3.974] $P < .0001$) and infectious disease (1.1%) (RR 18.33 [5.80–57.87] $P < .0001$). No significant difference was noted between the prevalence of bacteremia in oncology (21.3%) and HGE (16.2%). The prevalence of bacteremia in HGE was also significantly higher when compared to internal medicine / geriatrics (7.7%) (RR 2.1 [1.269–3.476] $P = .0014$), infectious disease services (1.1%) (RR 14 [4.394–44.610] $P < .0001$), and neurology (6.5%) (RR 2.471 [1.445–4.225] $P = .0003$. In contrast, the prevalence of PICC-line bacteremia in cardiology (13.1%) was significantly higher than that of infectious disease (1.1%) (RR 11 [3.524–36.45] $P < .0001$), "other medical specialties" (8.5%) (RR 1.909 [1.174–3.104] $P = .0038$), and neurology (6.5%) (RR 2.471 [1.445–4.225] $P = .0003$), but lower than that of oncology (21.3%) (RR 0.61 [0.41–0.91] $P = .0072$). Patients from infectious diseases had the lowest prevalence of bacteremia on PICC-lines at 0.66%. When we consider the yearly prevalence rate of bacteremia per PICC-lines inserted and by unit, hematology: 6.17% (20/324), oncology: 4% (55/1375), and HGE 3.6% (42/1142) had the highest prevalence of bacteremia per inserted PICC-line. In this context, cardiology accounted for only 2.26% (34/1498) bacteremia per inserted PICC-line. The units where the prevalence of bacteremia by inserted PICC-line was significantly lower were infectious diseases with 0.66%, followed by "other surgical services" with a rate of 0.71%, and finally internal medicine / geriatrics with 1.75%. The correlation analysis, when adjusted by exposure and year, shows that the service profile explains 72% of the variability in the rate of bacteremia with $P = .023$. The higher the risk profile of the service, the higher the bacteremia rate.

3.4. Delay between PICC-line insertion and bacteremia (Fig. 4)

Distribution of cases showed that the highest number of bacteremia occurred on day 2, with 32 cases 48 hours after insertion of the PICC-line (Fig. 4 left upper quarter). Then, the number of cases gradually decreased with a late episode between D26-D29. The mean time between insertion and bacteremia is 20 days with a median of 13 days. The 75% of bacteremia cases (194/257) occurred in the first 21 days after insertion. Distribution of bacteremia according to services is similar than above for oncology and HGE. However, for hematology, cases of bacteremia appear later, most often between D7 and D12. The distribution of bacteremia in cardiology and internal medicine/geriatrics was very different, with a late distribution of cases. On day 21, only 40% of cases were found, with 90% of cases appearing after 10 days.

3.5. Mortality observed in bacteriemic patients and controls: (Table 3)

The overall 30-day mortality of patients with a PICC-line was 1369/11334 or 12.07%. Mortality of patients with bacteremia

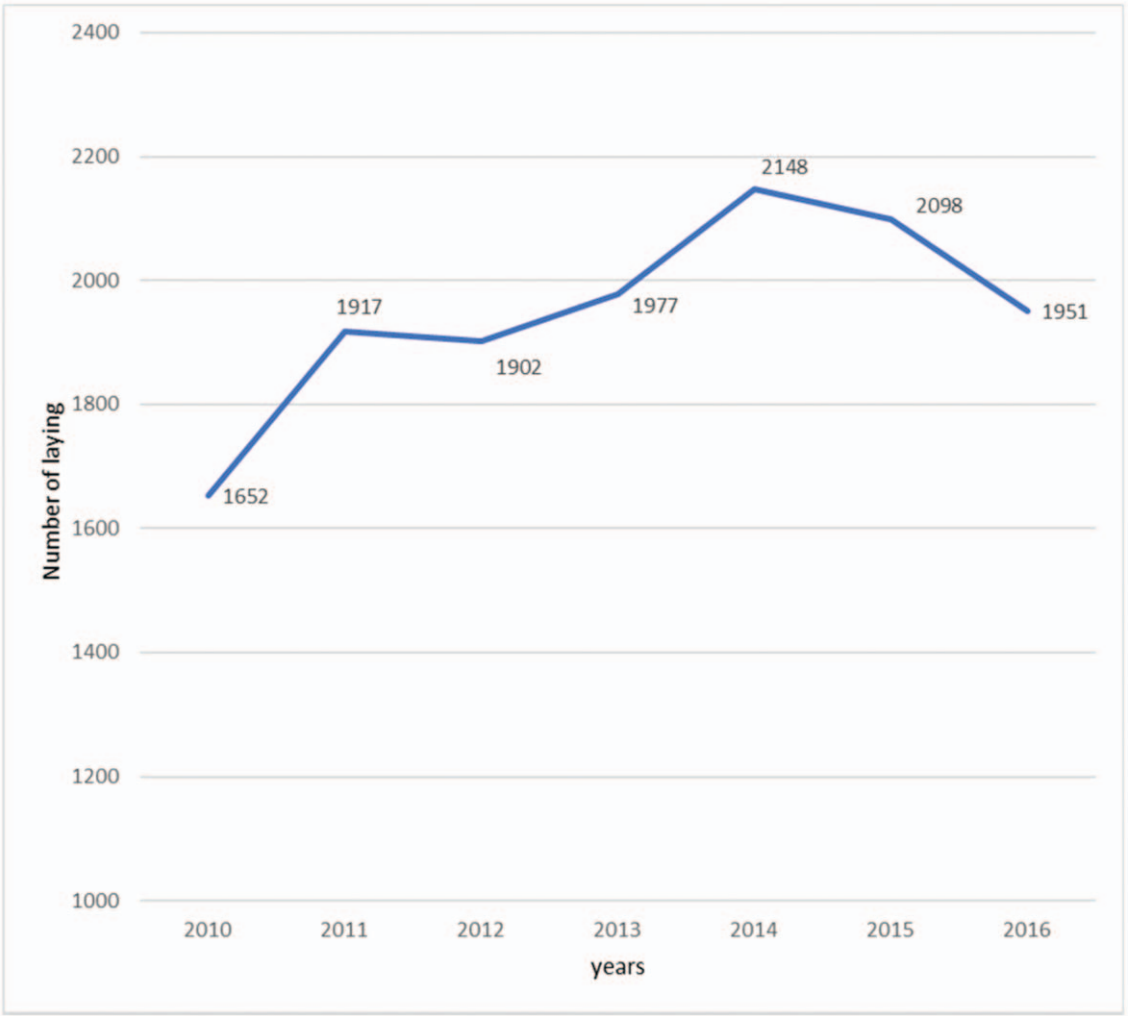

Figure 2. Evolution of the number of PICC-lines inserted each year 2010–2016.

was significantly higher 22.09% (57/258) than that of the control group 11.83% (1311/11076) (RR 2.066 [1.54–2.75] $P < .05$). In cardiology, the 30-day mortality was 24.56% (14/57), followed by oncology 19.29% (11/57); HGE 12.28% (7/57) and comparable with other "medical specialties" (Table 4). The lowest rates were observed for infectious diseases, neurology and palliative care services at 1/57 (1.75%) for each. The 30-day mortality from oncology was significantly higher than others: hematology (RR 3.667 [1.079–12.46] $P = .022$), infectious diseases (RR 11 [1.465–82.46] $P = .0023$) and neurology (RR 11 [1.465–82.46] $P = 0.0023$). Similarly, the 30-day mortality in cardiology was significantly higher than in hematology (RR 4.667 [14.417–15.37] $P = .0038$), infectious diseases (RR 14 [1.903–103.0] $P. = .0003$), internal medicine (RR 2.80 [1.080–7.262] $P = .00237$) and neurology (RR 14 [1.903–103.0] $P = .0003$). Mortality in bacteriemic patients per number of inserted PICC-Line showed the highest rate in cardiology 0.93% (14/1498), hematology with 0.92% (3/324), oncology 0.80% (11/1375) and both HGE along with other medical specialties 0.61% (7/1142). The lowest observed case-fatality rate is in the other surgical specialties 0.12% (3/2386), followed by neurology 0.14% (1/688) and infectious disease 0.22% (1/453).

3.6. Death delays in patients with bacteremia on the PICC-line

Among patients with bacteremia, 24/57 (42.10%) died in the first 6 days with an acme on day 3 (7 deaths). Another peak in mortality was also visible on day 9 after bacteremia with 5 deaths. Between D1 and D10, 63.15% patients died (36/57). The survival analysis showed a significant excess in mortality between the patients with a PICC-line associated bacteremia and controls (hazard ratio 1.89 [1.307–2.709] $P < .0007$) (Fig. 5). Excess mortality appearing at day 10 after the PICC-line is inserted. At 30 days, the survival rate was 81.39% in the group of patients with bacteremia on the PICC-line compared to 88.52% in the group of carriers of the PICC-line without bacteremia. At D15, the survival rate in the bacteriemic group was 87.98% compared to 91.04% in the group of PICC-line carriers without bacteremia.

3.7. Ecology of bacteremia on PICC-lines (Figs. 6 and 7)

We found a clear majority of coagulase negative *Staphylococci* 46.51%; followed by Enterobacteriaceae 23.25%, *Staphylococcus aureus* 11.24 and 5.42% (14/258) *Enterococcus sp*. Mortality by microorganism has the same distribution as above,

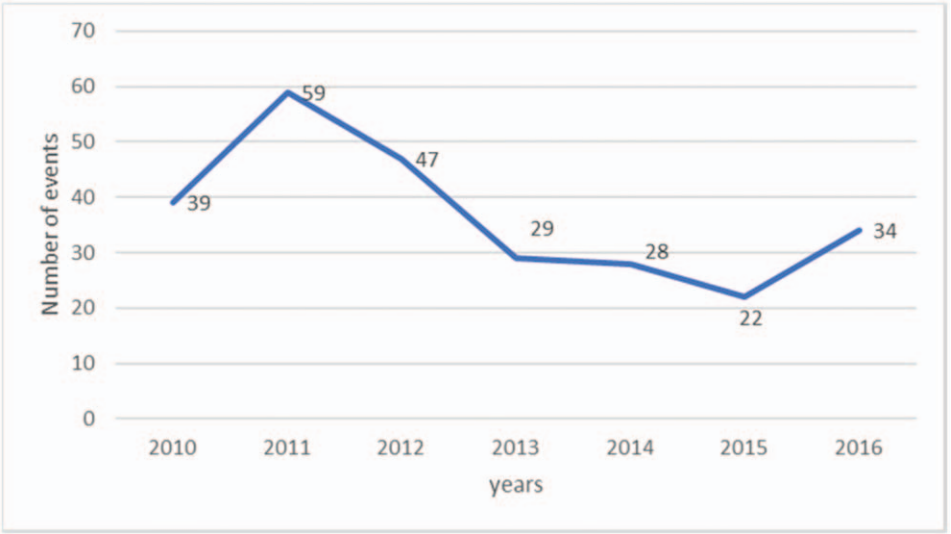

Figure 3. Yearly prevalence of PICC-lines-associated bacteremia [nb].

there was a statistical difference between the identified mortality and the mortality due to these bacteria ($P=.083$).

4. Discussion

The literature on catheter bacteremia is abundant, especially on the PICC-line, but is often related to ICU,[2,3,6,36–41] oncology[34,42–44] and pediatric oncology.[45] According to these studies, the PICC-line presents a risk of bacteremia higher[3,20,46] or inferior[21,47] to the classic central venous routes. These discrepancies relied on the fact that the population studied is very heterogeneous, and consequently the data are difficult to extrapolate. This registry study highlights several important and relatively new elements. To our knowledge, it is the only single-center study involving four university hospitals over such a long period (7 years) and studying mortality in all departments of the same structure, including medical and surgical services. The only study with higher numbers was the one conducted by Herc et al,[32] which recorded 249 episodes of PICC-line bacteremia over 23,000 exposures in 48 different Michigan hospitals. It included only medical services and did not evaluate the mortality induced by these episodes of bacteremia. In our institution, PICC-line insertion is performed by radiologists in radiology departments only, under the environmental conditions of interventional radiology. This allows us to have a comprehensive and consistent knowledge of all poses. Our study shows a very significant increase in the demand for PICC-lines in our institution, with an average insertion of 1950 devices per year, that is, a total of 13645 PICC-lines laid in 7 years. Prior to 2010, PICC-line insertions did not exceed 600/year. Although we do not have an exhaustive list of PICC-line break indications, we estimate, from our experience, that one third of the requested PICC-lines are outside the indications recognized by the French Society of Hospital Hygiene, thus resulting in a probable over prescription of this device.

Some medical units are identified as major PICC-line prescribers. The surgeries cumulate 30% of demands, followed by oncology, hepato-gastro-enterology and cardiology. Although

Table 2

Distribution of bacteriemic cases on PICC-lines by service: number and yearly prevalence and overall prevalence.

Bacteremia	Yearly prevalence, n (%)							Overall Prevalence, n (%)
Specialty	2010, n=39	2011, n=59	2012, n=47	2013, n=29	2014, n=28	2015, n=22	2016, n=34	258
Oncology	13 (33.33)	8 (13.55)	9 (19.14)	8 (27.58)	8 (28.57)	6 (27.27)	3 (8.82)	55 (21.31)
Hematology	2 (5.12)	6 (10.16)	4 (8.51)	3 (10.34)	2 (7.14)	1 (4.54)	2 (5.88)	20 (7.75)
Other surgical specialties	4 (10.25)	4 (6.77)	2 (4.25)	0	4 (14.28)	0	3 (8.82)	17 (6.58)
Other medical specialties	3 (7.69)	7 (11.86)	7 (14.89)	2 (6.89)	0	0	3 (8.82)	22 (8.52)
Cardiology	6 (15.38)	10 (16.94)	2 (8.51)	2 (6.89)	5 (17.85)	4 (18.18)	5 (14.70)	34 (13.17)
Gastro-intestinal and general surgery	4 (10.25)	4 (6.77)	3 (6.38)	2 (6.89)	1 (3.57)	2 (9.09)	8 (23.52)	24 (9.30)
Hepato-gastro-enterology	4 (10.25)	10 (16.94)	9 (19.14)	5 (17.24)	4 (14.28)	5 (22.72)	5 (14.70)	42 (16.27)
Infectious diseases	0	0	1 (2.12)	1 (3.44)	0	0	1 (2.94)	3 (1.16)
Internal medicine / geriatrics	2 (5.12)	7 (11.86)	5 (10.63)	1 (3.44)	2 (7.14)	2 (9.09)	1 (2.94)	20 (7.75)
Neurology	1 (2.56)	2 (3.38)	4 (8.51)	3 (10.34)	2 (7.14)	2 (9.09)	3 (8.82)	17 (6.58)
Palliative care unit	0	1 (1.69)	1 (2.12)	2 (6.89)	0	0	0	4 (1.55)

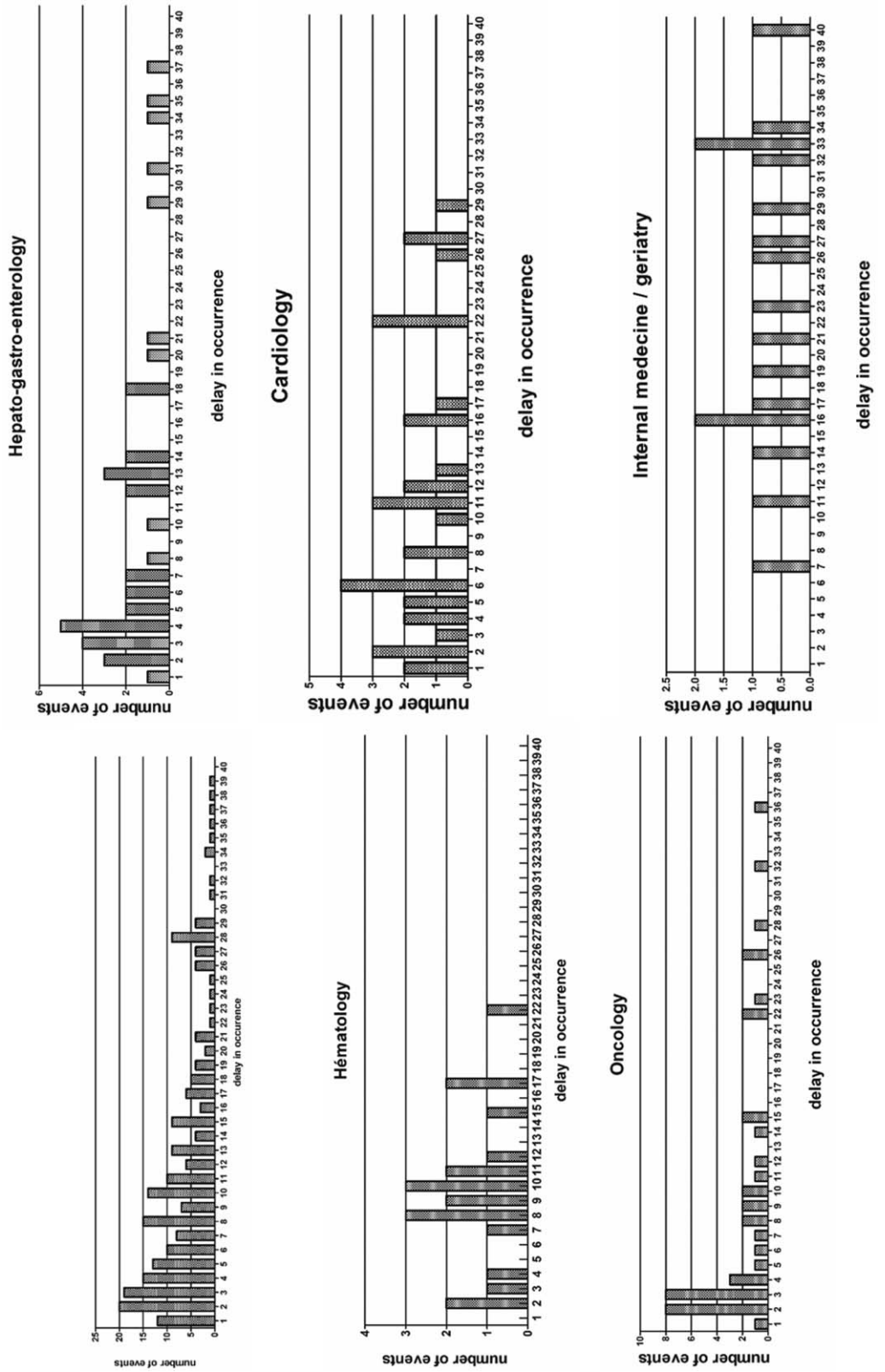

Figure 4. Number of events and time between PICC-line insertion (J-0) and diagnosis of bacteremia in the all cohort and in each service.

the study design does not allow medical indications for each insertion of PICC-line, in infectious diseases and internal medicine/geriatrics, the most common prescription is prolonged IV antibiotic treatment of bone infections, infectious endocarditis and deep wound infections. On the contrary, the oncology and hepato-gastro-enterology departments frequently use these

Table 3

Trends in mortality at 30 days among PICC-lines carriers, regardless of bacteremia and comparison of patients with PICC-line associated bacteremia and control.

	2010	2011	2012	2013	2014	2015	2016	Total
Mortality at 30 days in patients with a PICC-line	202/1330 (15.18%)	208/1547 (22.03%)	171/1655 (10.33%)	167/1600 (10.43%)	214/1859 (11.51%)	240/1748 (13.72%)	167/1595 (10.47%)	1369/11334 (12.07%)
Mortality at 30 days of patient with a PICC-line associated bacteremia	15/39 (38.46%)	13/59 (22.03%)	9/47 (19.14%)	9/29 (31.03%)	0/28	6/22 (27.27%)	6/34 (17.64%)	57/258 (22.09%)
Mortality at 30 days of patient with a PICC-line with no history of bacteremia (controls)	187/1291 (14.48%)	195/1488 (13.10%)	162/1608 (10.07%)	158/1571 (10.05%)	214/1831 (11.68%)	234/1726 (13.55%)	161/1561 (10.31%)	1311/11076 (11.83%)
P	*P* < .05	*P* < .05	*P* < .05	*P* < .05	*P* < .05	*P* < .05	*P* = .08	*P* < .05
RR	*1.856 [1.057–3.26]*	*1.819 [1.003–3.309]*	*2.055 [1.004–4.45]*	*3.86 [1787–8.34]*		*2.35 [0.93–5.96]*	*1.832 [0.76–4.36]*	*2.066 [1.54–2.75]*

RR = relative risk.

Table 4

Mortality in patients with bacteremia on PICC-lines per year and per specialty at 30 days.

	Annual mortality: n (%)							Overall mortality: n (%)
Specialty	2010, n = 15 (100)	2011, n = 13 (100)	2012, n = 9 (100)	2013, n = 9 (100)	2014, n = 0 (100)	2015, n = 6 (100)	2016, n = 6 (100)	Total, n = 57 (100)
Oncology	3 (20)	2 (15.38)	1 (11.11)	3 (33.33)	0	1 (16.66)	1 (20)	11 (19.29)
Hematology	0	0	1 (11.11)	2 (22.22)	0	0	0	3 (5.2)
Other surgical specialties	1 (6.66)	1 (7.69	0	0	0	0	1 (20)	3 (5.2)
Other medical specialties	2 (13.33)	2 (15.38)	2 (22.22)	0	0	0	1 (20)	7 (12.28)
Cardiology	2 (13.33)	5 (38.46)	1 (11.11)	1 (11.11)	0	3 (50)	2 (40)	14 (24.56)
Gastro-intestinal and general surgery	2 (13.33)	1 (7.69)	1 (11.11)	0	0	0	0	4 (7.017)
Hepato-gastro-enterology	2 (13.33)	1 (7.69)	1 (11.11)	1 (11.11)	0	1 (16.66)	1 (20)	7 (12.28)
Infectious diseases	0	0	1 (11.11)	0	0	0	0	1 (1.75)
Internal medicine / gériatrics	1 (6.66)	1 (7.69)	1 (11.11)	1 (11.11)	0	1 (16.66)	0	5 (8.77)
Neurology	1 (6.66)	0	0	0	0	0	0	1 (1.75)
Palliative care unit	0	0	0	1 (11.11)	0	0	0	1 (17.75)

catheters for the administration of parenteral nutrition. The increase in the use of PICC-line in our institution can be explained in several ways; the absence of a prescription controlled by a physician, an undeniable utility in the administration of intravenous parenteral nutrition products or antibiotic therapy, which can be a real comfort for the patient, and a poor knowledge of indications and recommendations of good practice.[12,15,29,30] Very often, parenteral nutrition is initiated on PICC-line, while a gastrostomy could be proposed in first intention.

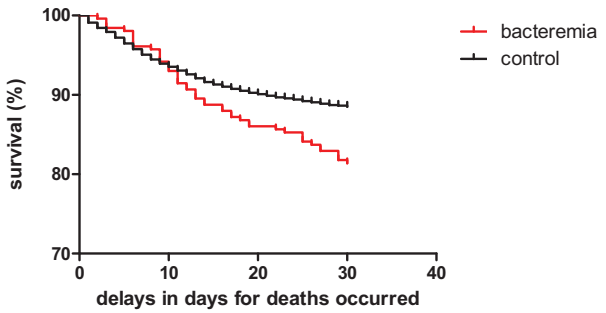

Figure 5. Comparative mortality and time to death in patients with PICC-line bacteremia and in patients with PICC-line without bacteremia episodes (control), by Kaplan–Meier survival analysis. J0 is the PICC-line insertion in both populations.

The second observation is the overall prevalence rate which is higher (2.27%) than the one found in some large series such as the one conducted by Herc et al, which reported an infection rate of 1.1%.[32] The very significant decrease in the prevalence rates of PICC-line infections from 2013 cannot be explained solely by changes in procedures, interventional radiology block or providers, since these are the same since 2010. The poses remained the same throughout the study period. This difference can, however, be explained by a major effort to train health care personnel, including the training of nurses for maintenance and more rigorous monitoring of the PICC-line. The training of prescribing physicians in infectious diseases also took place as part of our consulting activity in our institution. With the participation of infection control team, trainings and sensitization to the handling and the problems of period studied, it should be noted that the PICC-line models have presented a modification in their architecture, with the implementation of a neutral pressure check valve (MicroCLAVER). These valves would have a lower risk of PICC-line contamination and bacteremia.[48] Note that in our institution only PICC-line single-lights are installed by radiology departments. It is important to note that our data show that much of the reduction in PICC-line-associated bacteremia mortality has been achieved in hematology and, to a lesser extent, oncology. The weight in the overall reduction of bacteremia associated with the PICC-line significantly depends on hematology and oncology.

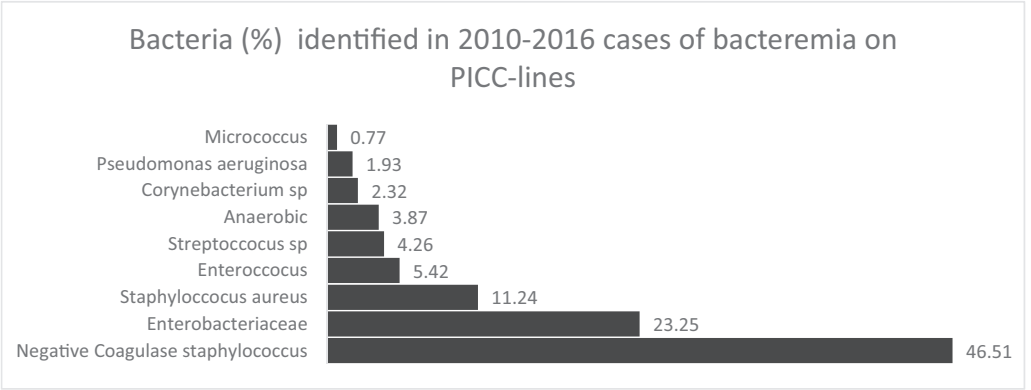

Figure 6. Bacteria identified as causative organism of bacteremia on PICC-lines from 2010-2016.

Correlation analysis identifies high-risk services and clearly demonstrates that PICC-lines in oncology, hepato-gastroenterology and hematology services are most likely to be the cause of bacteremia, independently of the PICC-line installation number. This implies an intrinsic overuse of these services, most likely a patient with a poor general condition, and requiring aggressive therapies, at risk of bacteremia such as parenteral nutrition. These data are consistent with literature found on this subject.[32,36] However, our results show that these same services are the ones that have contributed the most to the decrease of bacteremia since 2012, like hematology. Finally, the low prevalence reported in infectious disease might be due to the awareness of infectious disease physicians on infectious consequences and the specific use of PICC-line for antibiotic infusions.

The most prominent data highlighted in this work are the mortality data. In the same series, when we consider the total number of CRBSI occurring in patients with PICCs (1477 bacteriemic events, 9.8% of all the PICCs used) and the total number of bacteremia in patients without PICCs (10,413 bacteriemic events), the calculated risk of experiencing bacteremia was significantly higher in patients with PICCs (OR: 9.6, 95% CI 9.08–10.18, P value $< .001$)" (Durant et al 2019 Submitted). In the PICC-line carrier population, whether or not they have bacteremia, mortality is very high, with nearly 10% of patients dying within 30 days of insertion. The interpretation of the latter is delicate and complex. Certainly, the retrospective nature of our work limits the interpretation of the data. The best would be a prospective cohort study or a randomized trial. Due to the poor general state of patients and their significant comorbidities, this leads to confusion bias.

Nevertheless, it highlights that patients receiving such a device are often in a very poor general condition, with many comorbidities, ranging from cancers to malnutrition and immunosuppression. The underlying diseases are known to be a risk of death.[31,32] In addition, the aggressive therapeutics (chemotherapies, parenteral nutrition) represent a significant risk of bacteremia.[26–29,42] They may be associated with other causes of death but were not investigated in the study. In our experience, bacteremia on PICC-line would double the risk of death within 30 days.

Moreover, this mortality appears to be early, which is new compared to the data in the literature. Conventionally, the risk of bacteremia is associated with a prolonged duration of installation thereof and the number of handling. This duration is identified at 21 days in most studies.[2,36,49] It may be objected that the vast majority of these works involved the introduction of PICC-line in the intensive care unit or resuscitation unit. The result of our

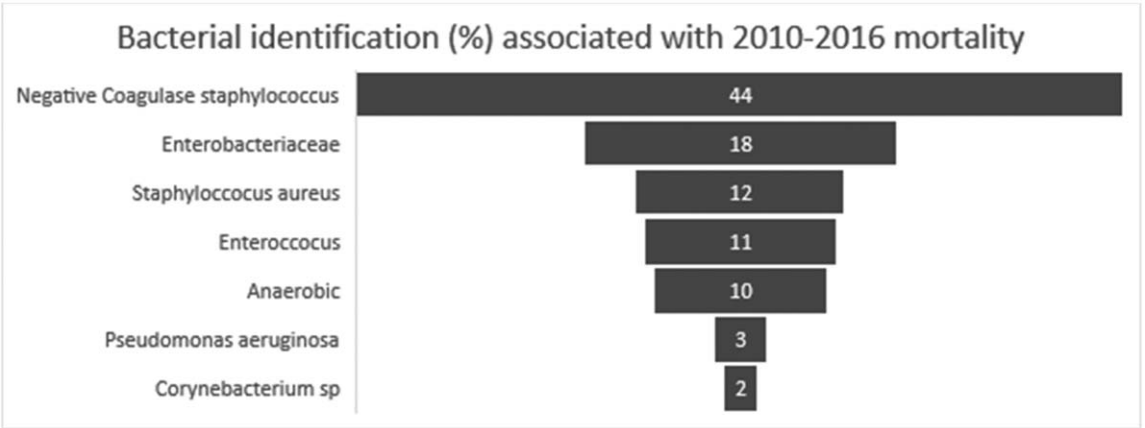

Figure 7. Bacteria considered as responsible for death in bacteriemic patients with PICC Line from 2010–2016.

study is possibly biased by the choice of inclusion criteria. It is likely that, by including only patients in a single hospital stay, we did not take into account some of the late bacteremia and their associated complications. Therefore, a patient receiving a PICC-line during a stay who would be complicated by a late infection after discharge was not included. In fact, a number of subsequent bacteremia events are probably not included in this study. On the other hand, PICC-line manipulations are generally much more frequent in hospitals which are risk factors for colonization and infection.[2,13,50,51] The findings of this study only provide an approximate estimate of prevalence and mortality rates, but the true figure may be higher or lower (underestimations or overestimations), particularly by design retrospective.

Our finding highlights another element relatively new. Indeed, the time of occurrence of bacteremia associated with PICC-line is very different according to the specialties. In some specialties such as hepato-gastroenterology, oncology or hematology where infection and mortality are relatively early; these profiles are similar to peripheral venous catheter infections. It should be noted that in these cases, the pose probably plays an important role in the occurrence of bacteremia. On the other hand, specialties such as cardiology and internal medicine have a spatial distribution of bacteria and mortality that is more spaced over time and much earlier. These data are more comparable to what has been observed in the literature. The bacterial ecology found in PICC-line bacteremia in our study dominated by gram-positive cocci, is very similar to what has been reported in peripheral venous and in central catheter infections. The study conducted by Wisplinghoff et al also showed 65% of gram-positive cocci infection (coagulase negative staphylococci and *S aureus*).[7] For us the most likely reason for the high incidence of coagulase-negative staphylococcal infections is the enhanced recognition and reporting of these organisms as valid bloodstream pathogens and the increased installation of long-term per-cutaneous equipment. The staphylococcal species are common constituents of the skin microbiota and could reflect the observation that central venous catheter infections are most commonly attributable to the patient's skin microbiota. In France, the National survey of resistance updated in February 2019 reports the 2017 Enterococcus resistance to vancomycin < 1%, extended-spectrum beta-lactamase enterobacteriaceae around 10%, and methicillin resistant *S aureus* in hospital at 12.9% (Santé Publique France).

5. Conclusion

PICC-lines, although having a large number of undeniable advantages, are not innocuous devices and their complications are relatively frequent. Over the past 7 years, 2.27% of 11334 PICC-line retains got complicated with bacteremia. Our findings suggest that patient with PICC-line associated bacteremia have a high risk of early mortality features not reported yet in the literature.

Ultimately, it is advisable to favor as much as possible other approaches, such as the *Per Os* treatment, or to propose implantable chambers (porta-cath) if the foreseeable duration of treatment will be greater than 3 months rather than PICC-lines Iterative. PICC-lines must remain a rare remedy for the administration of IV therapies. The indication of poses must be rigorously assessed, as well as the risk of complications, before making the decision to apply a PICC-line. To do so, a collegial discussion between confirmed practitioners should be the rule prior prescription. Due to the initial design of this study, these data must be supplemented by a prospective study including information on the indications for using PICC-lines and compliance with the recommendations.

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