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Peripherally inserted central catheter in patients with acute myeloid leukemia: incidence and risk factors for premature removal

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A reliable intravascular access, such as central venous catheters, is essential for acute myeloid leukemia (AML) patients treatment. The safe administration of chemotherapy and the immediate and intensive supportive care during intensive chemotherapy are critical in this high-risk population.

The use of peripherally inserted central catheter (PICC) has steadily grown over the years due to an easy placement and few perioperative complications, but related complications requiring anticipate removal, including catheter-related thrombosis (CRT), central-line-associated bloodstream infection (CLABSI), and mechanical complications, are reported [1,2]. Anticipate PICC removal, especially during chemotherapy-related aplasia, may question the safety of PICC use in AML patients, but data in this population are limited [3,4].

Cancer patients under chemotherapy have a high risk as for CLABSI as for CRT [1,2]. At the Hematology Department of Sapienza University of Rome, we observed a withdrawal rate of 26% in hematological patients who placed 1102 skin-tunneled centrally inserted central catheters (CICCs) and AML patients presented the major risk for early and late complications [3]. In 2009, we started to use PICC, the overall rate of PICC withdrawal was 25%, similar to our data on CICC [3], the 16.3% of AML patients developed CLABSI (1.07/1000 PICC days), and acute leukemia resulted independently associated to CLABSI while no factors resulted predictive for CRT [4]. An increased CRT risk was instead reported in AML patients receiving intensive chemotherapy with CVC exit-site infections and neutropenic sepsis [5]. In our experience on allo-HSCT recipients, PICC resulted a reliable long-term venous access: 68% of patients maintained the device for the entire transplant procedure, 44% without any PICC-related complications, CRBSI occurred in 32% of patients, CRT in 9% [6]. In hematological patients, PICC use compared to traditional CICC resulted associated

with a higher CRT incidence [7] while no great differences were reported on CLABSI occurrence [8–10]. However, in a randomized prospective study comparing CICC and PICC in AML patients receiving induction chemotherapy [11], infections and thrombotic rates were lower in PICC group resulting in about a fivefold risk reduction of CR-major complications during the first 30-day catheter *in situ* follow-up.

From September 2009 to December 2015, 312 PICCs were inserted in AML adult patients attending our Hematology Department. To evaluate incidence and risk factors for anticipate PICC removal, we retrospectively analyzed the first PICC inserted for intensive treatment in 144 AML patients. PICC inserted after the anticipate removal of the first PICC (no. 68) and PICC placed for supportive terminal care (no. 100) were excluded from the analysis.

A dedicated team of specifically trained physicians and nurses inserted PICC under ultrasound echography guide in the internal surgical facility or at patient bedside. PICC type and venous access (basilica or brachial vein) were decided according to guidelines [12]. No primary thromboprophylaxis and antimicrobial prophylaxis were routinely performed. A trained nursing staff performed weekly PICC medications and insertion site check (infection, hematoma, blockage, leakage occurrence).

PICC success was considered the maintenance of the device *in situ* until the end of need (end of treatment or death of the patient). PICC failure was considered the anticipate withdrawal because of any of the following complications: (a) CLABSI persistence, or fever, chills and patient clinical deterioration despite appropriate antibiotic therapy, or gram-negative, methicillin-resistant *Staphylococcus aureus*, *Candida* species CLABSI, or thrombophlebitis [13]; (b) CRT ultrasound evidence (vein incompressibility, absence of spontaneous flow, turbulent flow and presence of thrombotic material in the venous

Table 1. Patients and PICC characteristics.

Number of AML patients	144
Age, years (range)	57.4 (46.8–64.3)
Male	71 (49.3%)
Phase of AML	
Onset	95 (66.0%)
Uncontrolled disease	25 (17.4%)
Controlled disease	24 (16.6%)
Median PICC days (IQ range) ^a	83 (41–175)
Type of PICC	
Groshong	62 (43.1%)
Per-q-cat	27 (18.8%)
Power PICC	12 (8.3%)
Power Groshong	43 (29.9%)
Valve	
No	105 (72.9%)
Yes	39 (27.1%)
Materials	
Silicon	132 (91.7%)
Polyurethane	12 (8.3%)
Number of PICC lumen	
One lumen	131 (91.0%)
Two lumen	13 (9.0%)
French	
4 Fr	89 (61.8%)
5 Fr	55 (38.2%)
Arm of PICC insertion	
Right	130 (90.3%)
Left	14 (9.7%)
Vein of PICC insertion	
Basilical vein	116 (80.6%)
Brachial vein	28 (19.4%)
PICC inserter	
Doctor	67 (46.5%)
Nurse	77 (53.5%)

^aIQ range: interquartile range.

lumen) in symptomatic patients; (c) mechanical complications as dislocation, obstruction, malfunction (inability to infuse or withdraw after an initial period of a correct PICC function), breakage, leakage; (d) accidental removal.

Continuous variables were summarized using median and interquartile range, categorical variables using frequencies and percentages. Competing risk analysis was used to analyze the incidence of infection, thrombosis, mechanical complications, and accidental removal considered as competing risk events. The analyzed variables were: insertion on right vs. left arm, basilica vs. brachial vein use, type of PICC (PICC Groshong 4 Fr, PICC per-q-cath 5 Fr, Power PICC 5 Fr, Power PICC Groshong 5 Fr, Bard Access-Systems, Salt Lake City, UT), AML phase (onset vs. relapse vs. remission), one vs. two PICC lumen. The differences between groups were evaluated by the Gray test. A significance level of .05 was used. The statistical software R (version 3.5.2) was performed for all the analyses.

The total PICC days were 17,426, the median duration of PICC use was 83 days (IQ range 41–175, range 0–365 days, one patient died the day of PICC insertion).

Characteristics of AML patients and PICCs are shown in Table 1. Overall, PICC success was observed in 96 of 144 (67%) AML patients (median duration of PICC usage: 34 days, IQ range 32–90, range 0–34): 49 of 96 patients (51%) maintained the PICC for all the scheduled treatment (33 placed PICC at AML onset for intensive

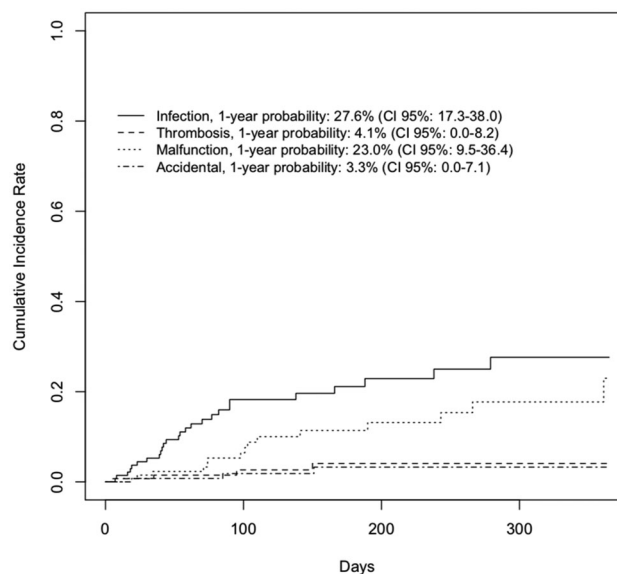


Figure 1. Risk analysis of incidence of infection, thrombosis, mechanical complication (malfunctions), and accidental removal, causing PICC failure.

induction therapy, 10 for intensive consolidation therapy, six for AML relapse treatment), 47 of 96 patients (49%) died for reasons other than PICC-related complication, with an *in situ* working device.

PICC failure occurred in 48 of 144 (33%) patients (median time to PICCs removal: 72.5 days, IQ range 37–124, range 5–361). Anticipate removal occurred during the aplastic phase in the 54% of patients but the 81% of patients underwent to a new PICC insertion without contraindications and/or complications.

Overall, 32 CLABSI were documented (22% of PICC, 1.8/1000 PICC days), during chemotherapy-induced neutropenia in 18 patients (69%). Gram-positives were involved in 17 cases (53%), Gram-negatives in 13 (41%), Candida in 2. CLABSI led to PICC removal in 26 cases (81% of CLABSI, nine Gram-negative, two Candida, and 15 persistent Gram-positive CLABSI, in six cases associated with vein thrombosis). Overall, CLABSI caused PICC removal in the 18% of the 144 PICC analyzed, and represented the 54% of PICC failures cases (26 of 48). CLABSI never represented the primary cause of death, two patients had a fatal sepsis originated from a documented distant source that contaminated the PICC. The median interval from PICC insertion to CLABSI was 56 days (range 7–365), to removal 53.5 days (range 7–279). The 1-year cumulative incidence (CI) of removal for CLABSI was 27%, and the majority of CLABSI occurred during the first three months (Figure 1). The CI of CLABSI shows no differences for the variables analyzed. A trend toward a CLABSI increased risk was observed for PICCs placed in brachial vein ($p=.08$), left arm ($p .09$), and double lumen PICC ($p=.054$).

CRT occurred in 18 patients (12.5% of PICC analyzed). Low-molecular-weight heparin was administered in all

patients but three with $<30 \times 10^9/L$ platelet count not responding to platelets transfusion. PICC was removed in four of 18 CRT (22%) for treating physician decision. CRT caused the removal of 2.7% of the 144 PICC analyzed and represented the 8% of PICC failures cases. No episode of pulmonary embolism occurred. The 1-year CI of removal for CRT was 4.1% (Figure 1).

Mechanical complications requiring the immediate removal of the unusable PICC occurred in 15 patients (10% of 144 PICC analyzed, 31% of PICC failure cases). The median time between PICC insertion and removal was 101 days (range 13–361), the 1-year CI of removal 23% (Figure 1).

Accidental PICC removal occurred in three cases with a 1-year CI of removal of 3.3%.

AML patients with PICC placed for intensive chemotherapy administration represent the population with the highest risk of PICC failure. In our analysis, 67% of PICCs completed their usage successfully, remaining in place without complications until the end of the scheduled treatment, notably one-third of PICCs were placed at AML diagnosis, or the death of the patient. The 33% of PICCs were removed for a complication when the device was still necessary; we have not found factors associated with PICC withdrawal except for trends toward CLABSI increased risk.

CLABSI, occurred in most cases during neutropenia, represented the first cause of PICC failure responsible of the 18% of PICC withdrawn. PICC was removed in the majority of CLABSI, however, since Gram-positives represented the most frequent cause, appropriate antibiotic treatment may cure the infection and/or delay the removal until the hematological recovery, reducing the rate of PICC failures particularly during the neutropenic phase [14]. The scarcity of multi-lumen PICC inserted may explain the absence of a clear association between multi-lumen PICCs and higher risk of infections, documented by others [2].

The intensive PICC use for chemotherapy and supportive treatment in AML patients could explain the high rate of mechanical complications occurring in the 10% of PICC analyzed, documented at any time during PICC stay in place. Moreover, a specific training for patient and caregiver could reduce failure cases related to incorrect PICC care during the discharge phase.

CRT caused the 2.7% of PICC withdrawn. Differently to the high rate of failures for CLABSI, PICC removal was decided only in the 22% of CRT cases and in the majority of patients, the device was retained without consequences, with or without low-molecular-weight heparin therapy.

In conclusion, in our experience, PICC represents a reliable intravascular access in AML patients, even during the most critical phases of intensive treatments. No life-threatening PICC-related complications were observed and the easy procedure of PICC insertion allowed a new

placement in patients who underwent anticipate PICC removal, even during aplasia.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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