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Identification of Targets for Prevention of Peritoneal Catheter Tunnel and Exit-Site Infections in Low Incidence Settings

Clara Santos,[1] Miguel Pérez-Fontán,[2,3] Ana Rodríguez-Carmona,[3] María Calvo-Rodríguez,[3] Andrés López-Muñiz,[3] Beatriz López-Calviño,[4] and Teresa García-Falcón[3]

Division of Nephrology,[1] Vilanova da Gaia/Espinho Hospital Center, Portugal; Health Sciences Faculty,[2] University of A Coruña, Spain; Division of Nephrology,[3] University Hospital of A Coruña, Spain; and Division of Epidemiology,[4] University Hospital of A Coruña, Spain

Abstract

Background. Peritoneal catheter tunnel and exit-site infection (TESI) complicates the clinical course of peritoneal dialysis (PD) patients. Adherence to recommendations for catheter insertion, exit-site care, and management of *Staphylococcus aureus* (SAu) carriage reduces, but does not abrogate the risk of these infections.

Objective. To reappraise the risk profile for TESI in an experienced center with a long-term focus on management of SAu carriage and a low incidence of these infections.

Method. Following a retrospective, observational design, we investigated 665 patients incident on PD. The main study variable was survival to the first episode of TESI. We considered selected demographic, clinical, and technical variables, applying multivariate strategies of analysis.

Main results. The overall incidence of TESI was 1 episode/68.5 patient-months. *Staphylococcus aureus* carriage disclosed at inception of PD (but not if observed sporadically during follow-up) (hazard ratio [HR] 1.53, $p = 0.009$), PD started shortly after catheter insertion (HR 0.98 per day, $p = 0.011$), PD after kidney transplant failure (HR 2.18, $p = 0.017$), lower hemoglobin levels (HR 0.88 per g/dL, $p = 0.013$) and fast peritoneal transport rates (HR 2.92, $p = 0.03$) portended an increased risk of TESI. Delaying PD $\geq$ 30 days after catheter insertion markedly improved the probability of TESI. Carriage of methicillin-resistant SAu since the start of PD was associated with a high incidence of TESI by these bacteria. On the contrary, resistance to mupirocin did not predict such a risk, probably due to the use of an alternative regime in affected patients.

Conclusions. Adherence to current recommendations results in a low incidence of TESI in PD patients. Interventions on specific risk subsets have a potential to bring incidence close to negligible levels. Despite systematic screening and management, SAu carriage is still a predictor of TESI. Antibiotic susceptibility patterns may help to refine stratification of the risk of TESI by these bacteria. Early insertion of the peritoneal catheter should be considered whenever possible, to reduce the risk of later TESI.

Keywords

Peritoneal catheter, peritoneal dialysis, Staphylococcus aureus, mupirocin, tunnel and exit-site infection

Infections affecting the tunnel and the exit-site of permanent peritoneal catheters (TESI) represent a significant source of morbidity and technique failure in peritoneal dialysis (PD) patients. These infections are able to progress to the peritoneal cavity and cause peritonitis (1), and may result directly in catheter removal and PD drop-out in a significant proportion of cases, despite significant advances in prevention and management during the last 2 decades (2).

Most previous studies addressing factors which may influence the appearance of TESI have focused on *Staphylococcus aureus* (SAu) carriage, catheter design and insertion techniques, and exit-site care procedures (2,3). Screening and treatment of SAu carriers is the single measure with a best defined impact on the incidence of TESI (4,5), although few PD experts would not concur with the statements that thorough catheter insertion, adequate surgical scarring, and dedicated exit-site care will help to prevent this complication (2,3,6-8). On the other hand, the information on other demographic or clinical factors with a potential impact on the incidence of TESI is limited, and often merged in the general topics of complications and survival of the peritoneal catheter. Establishing risk profiles for TESI in experienced settings could help at the time of planning further prevention strategies.

We have undertaken an observational analysis of a large cohort of patients treated with PD in an experienced center with a low incidence of TESI. Our main objective was to disclose risk subsets which could be a subject of specific interventions to reduce the incidence of this complication.

Population and Methods

General Design

Following a retrospective, observational design, we investigated the association of selected demographic, clinical and PD practice-related factors in patients incident on PD with the risk of developing TESI. The study setting was a tertiary hospital, University Hospital of A Coruña (UHAC), attending a median of 90 prevalent PD patients. The recruitment period was 1991 to 2011, and follow-up was closed by June 2013. This time lapse was selected due to a remarkable homogeneity of protocols for prevention of PD-related infections, with only minor changes introduced during the study period (see below). The main study variable was survival to the first episode of TESI. Control variables were recovered from a prospective database including all patients starting PD in our unit during the same period.

This study complied with the ethic requirements of our center for retrospective, observational studies.

Study Population

During the study period, 712 started PD in our unit. We considered 3 inclusion criteria:

1. Minimum follow-up of 3 months after catheter insertion
2. Minimum follow-up of 1 month on PD
3. Baseline and follow-up clinical records available

Six hundred and sixty-five patients fulfilled these inclusion criteria. The main characteristics of the study population are presented in Table 1.

TABLE 1
Main Demographic Characteristics of the Study Population

Age (years)	58.5±15.9 (8–87)
Gender (males/females) (%)	385/280 (57.9/42.1)
Kidney disease	
Glomerular	75 (11.3)
Interstitial	71 (10.7)
Vascular	59 (8.9)
Cystic	51 (7.7)
Systemic	23 (3.5)
Diabetic nephropathy	185 (27.8)
Other/Unknown	201 (30.2)
Diabetes mellitus (%)	224 (33.7)
Charlson's score	4.0±2.0 (2–11)
Origin (%)	
Incident	595 (89.5)
Hemodialysis	44 (6.6)
Failed kidney transplant	26 (3.9)
Initial modality of PD (%)	
CAPD	449 (67.5)
Automated PD	215 (32.3)
Secondary selection of PD (%)	79 (11.9)
Low socio-economic background (%)	216 (32.5)
Family-assisted PD (%)	270 (40.7)

PD = peritoneal dialysis; CAPD = continuous ambulatory PD; SD = standard deviation.
Figures denote mean values ± SD (range) (numerical variables) or absolute numbers (%) (categorical variables).

Main Clinical Procedures and Definitions

Systematic screening of SAu carriers and, when appropriate, PD partners (in cases of family-assisted PD) was performed during the full study period. Samples were taken in triplicate from both nares and the pericatheter area. An individual was defined as a carrier whenever any of these samples was positive for SAu. Carriers were treated with nasal (3 times daily) and (since 1994) daily pericatheter mupirocin for 7 days, and then screened every other month for recolonization. Should the latter occur, mupirocin was applied again. We screened routinely *in vitro* susceptibility of SAu to methicillin and mupirocin. Colonization by mupirocin-resistant strains was managed thereafter with 2% fusidic acid ointment. Non-carriers were scrutinized for SAu yearly, and entered to the carriers protocol whenever a positivity for SAu was detected during follow-up.

The following procedures have remained essentially unchanged during the study period. We used swan neck, double-cuff peritoneal catheters. Insertion was routinely carried out by a nephrologist. Surgical insertion was restricted to patients with suspected peritoneal adherences or needing a simultaneous surgical procedure. We administered cefazolin as antibiotic prophylaxis for catheter insertion. A delay of at least 2 weeks between insertion and initiation of PD was intended, but earlier initiation of PD was often preferred to central venous catheter-based hemodialysis. We protected the surgical wound and catheter exit site with closed dressings during 2 weeks after catheter insertion; this dressing was changed every 4 days before 2002, and weekly thereafter. Routine exit-site care was usually based on povidone iodine, with 2% saline or simple cleansing with soap and water reserved for specific indications (e.g. skin irritation).

We used integrated Y systems for continuous ambulatory PD, and Home Choice (Baxter, Deerfield, IL, USA) cyclers for automated PD. We used classic PD solutions in the majority of cases; low-glucose degradation product solutions were introduced after March 2008.

The diagnosis of peritonitis followed accepted standards (8). Tunnel and exit-site infection was diagnosed in the presence of at least 1 of: purulent discharge from the exit site, a combination of persistent serous or serohemorrhagic discharge plus a microbial isolation from the exit site, or the presence of overt signs of inflammation either around the exit site or in the subcutaneous catheter tunnel path. Mild, non-exudative inflammatory signs around the exit site were not recorded as infections. We do not routinely use tunnel sonography for routine screening or diagnostic work-up of TESI. Systemic antibiotics were used, according to *in vitro* susceptibility, for treatment of most TESI. Topical management was based on hypertonic saline, 0.3% ciprofloxacin solution, 0.3% gentamycin solution or 2% mupirocin ointment, as needed. Traumatized or equivocal exit sites were treated with topical 0.3% ciprofloxacin 2 times daily for a minimum of 5 days.

Study Variables and Laboratory Methods

The study variables were survival to the first episode (main) and incidence of TESI. We selected the catheter insertion date, rather than the PD initiation date, as the starting point for survival analyses.

The baseline control variables scrutinized were: age, gender, kidney disease, diabetes, PD vintage, origin (conservative, failed transplant, hemodialysis), PD modality and solution (third month), SAu carriage, comorbidity (Charlson's score), malnutrition (subjective global assessment), socioeconomic background, ability for self-dialysis, body mass index, hemoglobin, albumin (autoanalyzer), glomerular filtration rate (mean of urea and creatinine clearances), peritoneal transport (D/P ratio of creatinine at 240' D/Pcrea) and C-reactive protein (Immunoturbidimetry, Roche Diag., Mannheim, Germany). We also scrutinized the peritoneal catheter insertion technique and the delay between catheter insertion and initiation of PD.

Strategy of Analysis and Statistics

The main objective was to establish a predictive profile for TESI between catheter insertion and end of follow-up or termination of PD. We first compared patients who did or did not suffer TESI during follow-up. We then compared survival to the first episode of TESI according to the different independent variables. As a third step, we performed multivariate, adjusted estimations of the risk of suffering TESI during follow-up.

Numeric variables are presented as mean ± standard deviation (SD), unless abnormally distributed (median with range). We used the Student *t*-test, ANOVA and Mann-Whitney test to compare numeric variables, and χ^2 distribution and Fisher's test for categorized variables. Univariate analysis of survival to first TESI was carried out using Kaplan-Meier plots (log rank). Multivariate survival to the first episode of infection was produced by stepwise Cox regression analysis. Patients were censored in case of death, kidney transplant, transfer to hemodialysis or loss to follow-up. The same strategy was applied to identify predictors of TESI by SAu and gram-negative bacteria. D/Pcrea (n = 377) and C-reactive protein (n = 490) were not available in a significant proportion of cases, and were analyzed in separate models.

We used the SPSS 19.0 (SPSS Inc., Chicago, IL, USA) software for data analysis.

Results

Overview

Analysis included 665 patients (Table 1). Two hundred and eighty-two patients (43.7%) carried SAu at the start of PD, of whom 46 (16.3%) did not show further positivity after a first course of mupirocin. On the other hand, 81 of 245 patients negative for SAu at the start of PD were positive for this bacteria at some point during follow-up, yielding a final accumulated incidence of SAu positivity of 56.2%. Only 18 patients (2.7% of all patients, 6.4% of carriers) had methicillin-resistant SAu (MRSAu) isolated at the start of PD, but 95 (14.3% of all patients) did so at least once during follow-up. Regarding mupirocin, resistance was a rare event among SAu until the late 1990s, increasing rather abruptly and then stabilizing in the ensuing years, for an accumulated incidence of 24.0% between 2000 and 2012. Unfortunately, our screening protocol did not differentiate low-degree (minimum inhibitory concentration ≥ 8 μg/mL) from high degree (minimum inhibitory concentration ≥ 512 μg/mL) resistance, although the former may have been more frequent than the latter. Resistance of SAu to mupirocin since the start of PD was a rare event *(n = 7)*.

We recorded 230 episodes of TESI in 176 patients (1 episode in 129 patients, 2 in 36 patients and more than 2 episodes in 11 patients), for an overall incidence of 1 episode/68.5 patient-months. Table 2 displays the etiologic spectrum of TESI. Peritoneal catheter removal was necessary in 55 episodes (23.9 %) of TESI, including 9 cases (3.9%) of permanent discontinuation of PD. Simultaneous or secondary peritoneal infection was the most usual indication for catheter removal in the presence of TESI.

TABLE 2
Etiologic Agents of TESI

	TESI
Staphylococcus aureus	92 (40.0)
Coagulase-negative *Staphylococcus spp.*	30 (13.0)
Streptococcus spp.	5 (2.2)
Other gram-positives	14 (6.1)
Enterobacteriaceae	29 (12.6)
Non-fermenting gram-negative bacteria	26 (11.3)
Polymicrobial	29 (12.6)[a]
Fungal	2 (0.9)
Negative culture	3 (1.3)
Total number	230

TESI = tunnel and exit-site infection.
[a] *Staphylococcus aureus* present in 9 cases

Univariate Analysis

Table 3 displays univariate comparisons according to the presence of TESI during follow-up. Univariate survival analysis (Kaplan-Meier) provided similar results, indicating that PD vintage ($p < 0.0005$), SAu carriage ($p = 0.001$), PD after transplant failure ($p = 0.02$), delay between catheter insertion and PD inception ≥ 30 days ($p < 0.001$) (Figure 1), and hemoglobin < 10 g/dL ($p = 0.02$) were associated with an increased risk of TESI, with non-significant trends for low socioeconomic status ($p = 0.07$) and fast peritoneal transport rates ($p = 0.057$).

TABLE 3
Univariate Comparisons According to TESI During Follow-Up

	TESI	No TESI	*p*
n	167	498	
Age (years)	57.6±16.1	58.7±15.9	0.44
Gender (% males/females)	55.1/44.9	58.8/41.2	0.40
Vintage (PD started before/after 2000) (%)	70.1/29.9	43.8/56.2	0.0005
Diabetes (%)	35.3	33.1	0.60
Charlson's score	4.0±1.9	4.0±2.1	0.89
Malnutrition (%)	12.0	10.2	0.53
Depression (%)	8.4	8.6	0.10
Immunosuppression (%)	9.6	8.0	0.53
Origin (%)			0.28
Incident	86.2	90.6	
Hemodialysis	8.4	6.0	
Failed kidney transplant	5.4	3.4	
Modality of PD (% CAPD/APD)	66.5/33.5	68.0/32.0	0.71
Secondary selection of PD (%)	14.4	11.0	0.25
Low socioeconomic background (%)	37.1	31.0	0.24
Assisted PD (%)	43.1	39.8	0.46
Follow-up (months)	38.6±25.4	26.4±24.0	<0.001
Staphylococcus aureus carriage (%)	54.3	38.6	<0.001
Peritoneal catheter insertion technique (% nephrologist/surgeon)	90.2/9.8	91.0/8.0	0.77
Delay catheter insertion-PD (days)	24.9±26.0	34.1±38.4	0.001
Body mass index (kg/m^2)	25.5±4.9	25.5±4.3	0.92
Plasma albumin (g/dL)	37.2±5.2	37.0±5.7	0.69
Hemoglobin (g/dL)	10.0±1.7	10.4±1.7	0.008
C-reactive protein (mg/dL)	0.84 (0.10–10.5)	0.55 (0.10–52.4)	0.008
Glomerular filtration rate (mL/m)	5.2±3.5	6.0±3.9	0.021
D/P creatinine 240', baseline PET	0.69±0.12	0.65±0.13	0.005

TESI = tunnel and exit-site infections; CAPD = continuous ambulatory PD; APD = automated PD; PD = peritoneal dialysis; SD = standard deviation.
Baseline variables. Figures denote mean values ± SD (numerical), median values (range) (C-reactive protein) or % of cases (categorical). Comparisons by Student *t*-test, ANOVA, Mann-Whitney and χ^2 distribution.

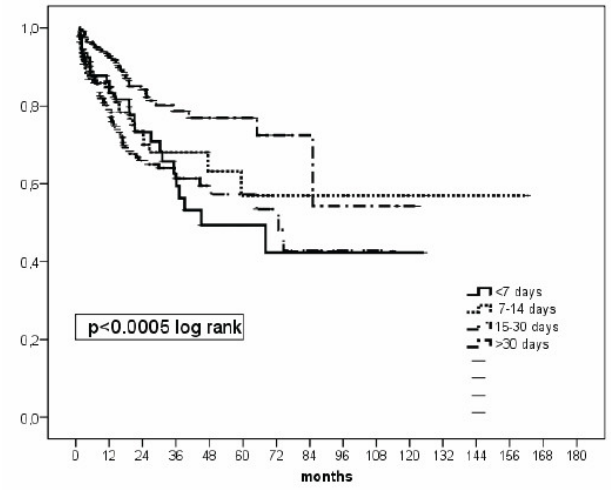

Figure 1 Survival to first episode of TESI according to delay between peritoneal catheter insertion and initiation of PD. TESI = tunnel and exit-site infection.

Multivariate Analysis

Cox's models confirmed PD vintage (Figure 2), SAu carriage, shorter delay between catheter insertion and initiation of dialysis, PD after kidney transplant failure, and lower baseline hemoglobin as independent predictors of TESI (Table 4). Importantly, categorization of delay between catheter insertion and initiation of PD showed that the improvement in the probability of TESI was not linear. A lapse ≥ 30 days (n = 225) was associated with a lower risk than < 7 days (n = 94) (HR 1.40, 95% CI 0.91 – 2.35, p = 0.13), 7 – 14 days (n = 110) (HR 1.69, 95% CI 1.03 – 2.79, p = 0.040), and, remarkably, 15 – 30 days (n = 222) (HR 1.94, 95% CI 1.29 – 2.95, p = 0.001). We did not detect significant interaction terms between the main study variables.

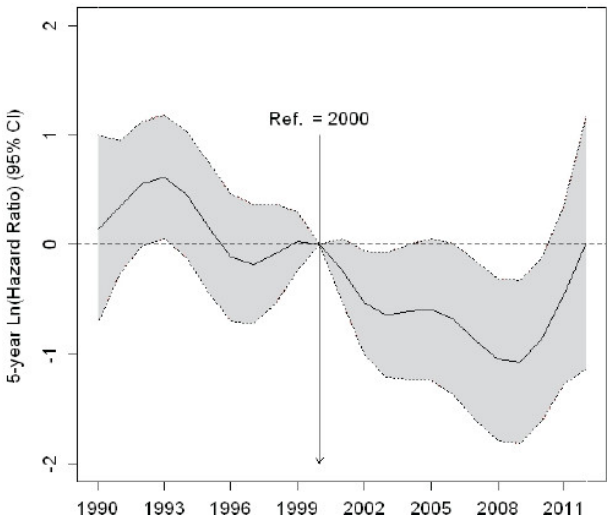

Figure 2 Hazard ratios of TESI by year of start of dialysis (modeled by splines with 7 degrees of freedom) and time of follow-up. Adjusted for main covariates ($p < 0.001$ Cox). TESI = tunnel and exit-site infection; CI = confidence interval.

TABLE 4
Multivariate Analysis (Cox's regression) of Baseline Predictors of TESI

	Hazard ratio	95% CI	*p*
Vintage (Ref. PD before 2000)	0.62	0.48–0.80	<0.0005
Staphylococcus aureus carriage (Ref. No.)	1.53	1.12–2.10	0.009
Delay between catheter insertion and initiation of PD (per day)	0.98	0.98–0.99	0,011
Modality before PD (Ref. Incident)			0.039
Hemodialysis	1.48	0.85–2.57	0.17
Kidney transplant	2.18	1.10–4.30	0.017
Baseline hemoglobin (per g/dL)	0.88	0.80–0.97	0.013

TESI = tunnel and exit-site infection; CI = confidence interval; PD = peritoneal dialysis.
Stepwise Cox regression analysis. Study variable: Survival to first episode of TESI. -2 log likelihood 1836.7. Global model χ^2 value 60.68, $p < 0.0005$.

Secondary models showed an increased risk of TESI for fast transporters (HR 2.92 vs low transporters, 95% CI 1.10 – 7.73, $p = 0.03$) (-2 log likelihood 817.3, global model χ^2 32.87, $p < 0.001$).

Subanalyses for Different Agents of Tesi

Tunnel and exit-site infection by SAu appeared earlier than those caused by gram-negative bacteria (15.8 ± 1.7 vs 21.2 ± 3.0 months, $p = 0.031$). Univariate analysis disclosed a roughly coincident risk profile between TESI by SAu and the general profile (Table 2). In terms of TESI by gram-negative bacteria, only fast peritoneal transport rates ($p = 0.026$) and higher C-reactive protein (median 0.95 vs 0.56 mg/dL, $p = 0.037$) sustained a significant association.

Staphylococcus aureus carriage was a predictor of TESI by SAu only when present since the start of PD, but not for patients negative at inception and positive during follow-up (Figure 3). The same applied for MRSAu (Figure 4). Appearance of resistance to mupirocin during follow-up did not portend an increased risk of TESI by SAu (p = 0.85, log rank). The impact of baseline resistance to mupirocin could not be explored due to the small size of the sample.

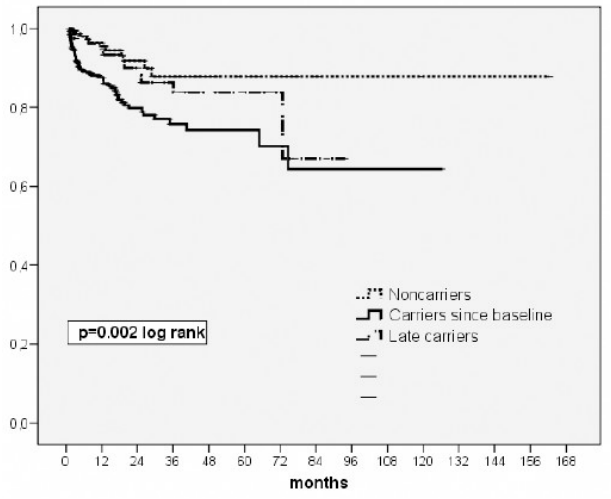

Figure 3 Survival to first episode of TESI by SAu according to carriage of SAu, either detected since inception of PD or later during follow-up. TESI = tunnel and exit-site infection; SAu = *Staphylococcus aureus*; PD = peritoneal dialysis.

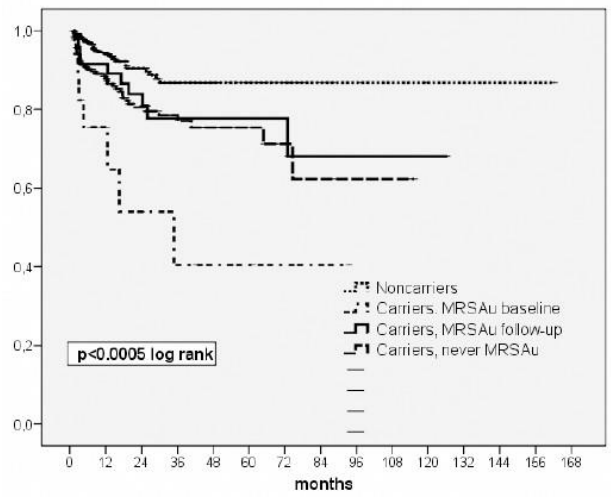

Figure 4 Survival to first episode of TESI by SAu according to carriage of MRSAu, either detected since inception of PD or later during follow-up. TESI = tunnel and exit-site infection; SAu = *Staphylococcus aureus*; MRSAu = methicillin-resistant SAu; PD = peritoneal dialysis.

Multivariate analysis identified SAu carriage (HR 1.97, 95% CI 1.25 – 2.95, $p = 0.006$), delay between catheter insertion and initiation of PD (HR < 7 days vs ≥ 30 days 1.77, 95% CI 1.12 – 3.03, $p = 0.04$), plasma albumin (HR 0.96 per g/dL, 95% CI 0.92 – 0.99, $p = 0.044$), and PD after transplant failure (HR 3.05, 95% CI 1.36 – 5.84, $p = 0.007$) as independent predictors of TESI by SAu. On the other hand, fast peritoneal transport (HR 1.05, 95% CI 1.02 – 1.08, $p = 0.003$) was the only consistent predictor of TESI by gram-negatives, with similar trends for lower glomerular filtration rate ($p = 0.07$) and hemoglobin levels ($p = 0.06$) but, in general, the study was underpowered to model adequately the latter complication.

Multivariate subanalyses for TESI by SAu confirmed that SAu carriage at inception (HR 2.49, 95% CI 1.28 – 4.78, $p = 0.007$) but not if observed later (HR 1.53, 95% CI 0.66 – 3.56, $p = 0.32$) portended a high risk of this complication. On the other hand, a similar, non-significant trend applied for carriage of MRSAu, with HR 2.19 (95% CI 0.96 – 4.83, $p = 0.07$) for carriers at the start of PD, as compared with HR 0.82 (0.41 – 1.86, $p = 0.59$) for late positivity (comparison with SAu carriers who were never positive for MRSAu). Resistance to mupirocin during follow-up did not carry a significant risk of TESI by SAu ($p = 0.87$).

Discussion

TESI represents a significant source of morbidity, technique failure and even mortality among PD patients (9). The incidence of these infections shows a remarkable variability among different centers (10-13). Adherence to recommendations for prevention and management (2,3,8) permits keeping the incidence of TESI in the vicinity of 1 episode every 5 patient-years, or even lower, as occurred in our unit. Even in this scenario, further reduction in the incidence of this complication is desirable. Exploration of demographic and clinical factors associated with a risk of TESI may help to refine prevention, once all the essential recommendations have been fulfilled.

There is a relative paucity of studies comprehensively exploring the risk profile for TESI. Moreover, a majority (10,14-16) were carried out during earlier years of PD and may not be representative of the current status of the problem. *Staphylococcus aureus* carriage has been a long-term subject of attention. Several randomized studies and metaanalyses indicate that mupirocin (4,5) and other antibiotic protocols (11,17) can markedly reduce the incidence of TESI, mainly by SAu, but also by other bacteria. On the other hand, studies addressing the role of technical factors have yielded less consistent results. An overview of these analyses suggests that neither the catheter type nor the insertion technique bear a clear influence on the later incidence of TESI (3), although double-cuff designs and downward orientation of the exit site offer some potential, not unequivocal advantages (2). Antibiotic prophylaxis for catheter insertion is more clearly endorsed by evidence (3). On the other hand, a minimal delay between catheter insertion and PD inception is advisable, to permit correct epithelization of the subcutaneous exit-site track (6). Two weeks is the International Society for Peritoneal Dialysis recommendation for this purpose (3). Finally, correct care of the exit site can also reduce the risk of TESI (14), although the optimal procedures (frequency of cure, types of disinfectant and dressing, etc.) have not been established (7).

Available information about how demographic and other clinical factors may influence the appearance of TESI is clearly insufficient. Older studies indicated that obesity (6), younger age (10,18) and a longer stay on PD (19) could favor the development of this complication. A recent report has suggested that new, biocompatible solutions may be associated with a lower incidence of TESI (20), although a before-after design limits the reliability of this finding. Tunnel and exit-site infection appears to be similarly frequent in patients treated with continuous ambulatory PD and automated PD (19,21).

Our study provides some potentially consequential clues to the question. Importantly, our data suggest that a delay of at least 1 month between catheter insertion and initiation of PD may be more appropriate to prevent TESI than the current International Society for Peritoneal Dialysis recommendation of 2 weeks (Figure 1) (3). These findings emphasize the convenience of permitting complete scarring of the catheter tunnel and exit site, and challenge the extended practice of holding off on catheter insertion until the need for dialysis is impending.

The decline in the incidence of TESI during the second half of the study period (Figure 2) suggests a global improvement in the quality of care protocols, which may not be captured by specific variables. On the other hand, and despite our long-term experience in screening and management (22), SAu carriage was still an independent predictor of TESI by the same bacteria. Several factors may have contributed to the persistence of this association. For instance, SAu carriage may signal patients with a predisposition to infection by this bacteria, which local nasal and pericatheter-oriented management may not reverse completely. In addition, the optimal approach for screening and treating carriers is yet to be established (23). On the other hand, in a previous study, we reported that resistance of SAu to mupirocin may favor TESI (24) but the use of an alternative regime (2% fusidic acid) appeared to abrogate this risk, in more recent years. Other regimes (11,18) may be similarly effective for this purpose, although the use of polysporin triple ointment may associate a deterrent increase in the incidence of fungal infections (18). Overall, our results support monitoring the susceptibility of SAu to agents used for eradication of this bacteria, as well as implementing alternative management strategies in case of resistance.

Isolation of MRSAu at the start of PD portended a particularly high risk of TESI by SAu during follow-up. Interestingly, the risk of TESI by SAu (or MRSAu) was restricted to patients incident on PD, but not for those positive during follow-up (Figures 3 and 4). The significance of this finding is not clear, but we suggest that our initial screening protocol (including sampling in triplicate) may be efficient to detect real, persistent carriers, as opposed to late isolations, which could reflect inconsistent or sporadic colonizations.

Patients starting PD after kidney transplant failure were at particular risk of TESI. Immunosuppression and deficient scarring likely contributed to this association. We are unaware of previous studies assessing this question, but the risk of peritonitis has been reported to be either similar (25) or increased (26) in these patients. A particular attention to early catheter insertion and postoperative wound and exit-site care is seemingly warranted in this setting.

Lower hemoglobin levels and fast peritoneal transport rates showed a consistent association with the probability of suffering TESI. The explanation for these findings is not clear. Anemia is a marker of comorbidity and poor general condition, which may set a generic predisposition to infection. We are unaware of previous reports relating fast creatinine peritoneal transport with the risk of infection in PD, but some studies have detected this association in patients with large pore dysfunction, a condition often linked to fast peritoneal transport (27,28).

Diabetics did not show an increased incidence of TESI, in agreement with former studies (29). A recent investigation from our unit suggested that the risk of TESI in diabetics may be linked to metabolic control (30). Surgical insertion of the peritoneal catheter did not carry a different risk of TESI than insertion by a nephrologist. This finding could be somewhat unexpected, because patients with a surgically inserted catheter had a more complicated profile, including preexisting abdominal disease, and simultaneous surgery.

Our study suffers significant limitations, including a retrospective, single-center design, which leaves open the possibility of bias by selection. Moreover, the homogeneity of clinical procedures prevented analysis of some potential risk factors for TESI, including catheter design and exit-site care procedures. On the other hand, this report provides clear insights into the risk profile for TESI in a low-incidence setting, pointing to some subsets of patients as targets for intensified prevention, and showing that early catheter insertion may be very effective to avoid this complication. The incidence of TESI in 104 patients initiating PD after 2000, who were not SAu carriers and who respected a delay of $\geq$ 30 days to start PD after catheter insertion was 1 episode/257.8 patient-months, close to negligible, suggesting that eradication of TESI as a concern in PD units may be a realistic objective.

In summary, TESI still complicates the clinical course of PD patients. Adherence to recommended clinical procedures markedly reduces the incidence of this infection. Categorization of high-risk subsets, including SAu carriers and patients starting PD after failure of a kidney transplant, may permit individualized interventions, to further reduce the impact of TESI. Particular attention should be paid to the susceptibility patterns of SAu to methicillin and antibiotics used for eradication of this bacteria (including mupirocin), and specific management strategies should be designed for resistant strains. Early insertion of the peritoneal catheter appears to be a very effective measure to reduce the later incidence of TESI.

Disclosures

All the authors contributed significantly to performing the investigation and/or constructing the manuscript. This investigation has not been published, nor is it under consideration for publication elsewhere, except in abstract form. Finally, the authors have no financial conflicts of interest to declare.

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