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Gram-negative bacterial colonizations before bilateral lung transplant. The impact of 'targeted' versus 'standard' surgical prophylaxis

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Abstract

Background Infections are one of the most common causes of death after lung transplant (LT). However, the benefit of 'targeted' prophylaxis in LT recipients pre-colonized by Gram-negative (GN) bacteria is still unclear.

Methods All consecutive bilateral LT recipients admitted to the Intensive Care Unit of the University Hospital of Padua (February 2016–2023) were retrospectively screened. Only patients with pre-existing GN bacterial isolations were enrolled and analyzed according to the antimicrobial surgical prophylaxis ('standard' vs. 'targeted' on the preoperative bacterial isolation).

Results One hundred eighty-one LT recipients were screened, 46 enrolled. Twenty-two (48%) recipients were exposed to 'targeted' prophylaxis, while 24 (52%) to 'standard' prophylaxis. Overall prevalence of postoperative multi-drug resistant (MDR) GN bacteria isolation was 65%, with no differences between the two surgical prophylaxis ($p=0.364$). Eleven (79%) patients treated with 'standard' prophylaxis and twelve (75%) with 'targeted' therapy reconfirmed the preoperative GN pathogen ($p=0.999$). The prevalence of postoperative infections due to MDR GN bacteria was 50%. Of these recipients, 4 belonged to the 'standard' and 11 to the 'targeted' prophylaxis ($p=0.027$).

Conclusions The administration of a 'targeted' prophylaxis in LT pre-colonized recipients seemed not to prevent the occurrence of postoperative MDR GN infections.

Keywords Surgical prophylaxis, Prophylaxis, Antimicrobial stewardship, Lung transplant, Bilateral lung transplant, Antibiotics

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Introduction

Infections are one of the most frequent complications of lung transplantation (LT) and the most common cause of death during the first year, with a mortality rate up to 37% [1, 2]. Overall prevalence of Gram-negative (GN) infections is annually increasing (4.33/1000 recipient-days) [3–6]. The prevalence of multidrug-resistant (MDR) GN bacteria is around 30% after LT, with an in-hospital mortality six times greater than recipients experiencing GN bacterial infections with no antimicrobial resistances [6, 7]. Long-term exposure to immunosuppression to prevent graft rejection has been recognized as the most relevant risk factor for increasing vulnerability to infections [8–10]. Therefore, even if antimicrobials may promote antimicrobial resistance, these medications remain life-saving medications [11].

The impact of both donor and recipient pre-existing colonizations on the occurrence of post-LT pneumonia and other infections is conflicting and debated [6, 12–16]. A relatively low risk of donor-recipient bacteria transmission (up to 2.9% of cases) has been reported and the presence of donor's organisms has not been necessarily associated with the occurrence of post-LT pneumonia [17]. On the other hand, it's known that pre-existing recipient's GN colonizations are an independent predictor of isolation of MDR GN bacteria after LT, despite not always being responsible for severe clinical conditions [7, 14, 18–23].

The optimal antimicrobial approach for pre-operative GN bacterial colonizations in LT recipients is still unclear. Noteworthy, the potential benefit of a personalized surgical prophylaxis, i.e. 'targeted' on preoperative colonizations, is still under discussion. The last guidelines reported conflicting data on the titration of antimicrobial prophylaxis based on previous colonization, while a watchful post-LT microbiological surveillance is always recommended for a prompt identification of infections requiring targeted antimicrobial therapies [15, 21–25].

Therefore, aim of this retrospective observational study, enrolling bilateral LT recipients pre-colonized by GN bacteria, was assessing: *(i)* the overall prevalence of MDR GN bacteria, over the whole bacterial isolates, within the first 30 days following bilateral LT; *(ii)* the prevalence of infections and colonizations due to MDR GN bacteria; and *ii)* the impact on short- and mid-term outcomes of the exposure to 'standard' or 'targeted' surgical prophylaxis (according to in vitro susceptibility).

Materials and methods

The study was approved by the Institutional Ethic Committee of Padua University Hospital (reference number 0025364) and was conducted in accordance with the principles of Good Clinical Practice and according to the Declaration of Helsinki. Written informed consent was obtained from all subjects and/or their legal representatives. The article was written in accordance with the "strengthening the reporting of observational studies in epidemiology-STROBE" checklist (Table S3) [26].. All consecutive patients admitted to our ICU at the Padua University Hospital after the first bilateral LT, between February 10th, 2016 and February 11th, 2023, were retrospectively evaluated and enrolled according to the following inclusion criteria: (1) age > 18 years; (2) written informed consent; (3) absence of invasive mechanical ventilation (IMV), extracorporeal membrane oxygenation (ECMO) and hospitalization before surgery; (4) documented pre-existing recipient-related GN bacterial isolations (Fig. 1). Patients underlined single or a second LT or exclusively pre-colonized by Gram-positive (GP) bacteria were excluded.

All screened LT recipients had at least one complete microbiological screening performed 6 months before surgery and all donor- and recipient-related pre-colonizations were confirmed by biological fluid samples collected perioperatively.

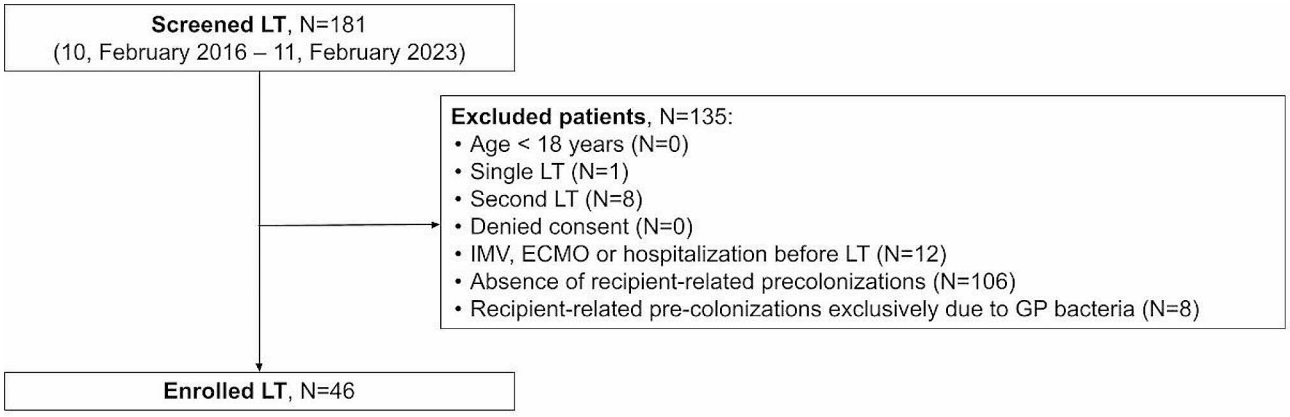

Fig. 1 Flow-chart. *Abbreviations*: LT, lung transplant; IMV, invasive mechanical ventilation; ECMO, extracorporeal membrane oxygenation; GP, Gram-positive

Standardized protocols for perioperative antibiotic management and immunosuppressant therapy were developed in our center following international recommendations and were previously published [6, 18, 21–23]. Specifically, the 'standard' surgical prophylaxis included intravenous piperacillin-tazobactam or ceftazidime, plus teicoplanin for GP bacteria. This strategy was followed from October 2020 until February 2023 and applied to all precolonized LT recipients without signs of sepsis or septic shock before LT. By contrast, the 'targeted' protocol was applied in a previous period of time (from January 2016 until September 2020) and allowed to use perioperative 'targeted' antibiotics, according to the preoperative bacterial isolates, and in vitro susceptibility testing following the European Committee on antimicrobial susceptibility testing (EUCAST) recommendations, in clinically stable LT recipients without signs of sepsis or septic shock before LT [27–32]. After ICU admission, a standardized protocol for microbiological surveillance has been constantly applied in our center service, until hospital discharge, as described in Table S4 and previously published [14]. Specifically, according to our surveillance protocol, we routinely collected, usually at the ICU admission and then every 2–3 days, bronchoalveolar lavage (BAL) and/or bronchoalveolar aspiration (BASP), blood and urine samples (expecially in case of infection), and rectal swabs (Table S4).

Gram-negative bacteria were classified as multisensitive (MS) or MDR according to the internationally recognised definitions [33–37]. Conventionally, our 'MDR'-group included carbapenem-resistant Enterobacterales (CRE), 'difficult-to-treat' *Pseudomonas aeruginosas* and carbapenem-resistant *Acinetobacter baumanii* (CRAB) [33–37].

The diagnosis of infection was clinically made according to the definition proposed by "The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)" and, microbiologically, according to the definitions provided by "CDC/NHSN Surveillance Definitions for Specific Types of Infections", as previously published [25, 38]. In case of bacteria isolation without (a) signs and symptom of infection, and (b) no meeting the microbiological criteria for infection, as described above, the patient was defined as colonized.

All variables collected from electronic health records were listed in Tables 1, 2 and 3 and S1 and S2.

Baseline characteristics of patients (collected from electronic health records) were summarized through descriptive statistics [number, proportion, median, interquartile range (IQR)]. Categorical variables were compared by chi-square ($\chi 2$), or Fisher exact test, when necessary. The Wilcoxon rank-sum test was used for the comparison of continuous variables. Statistical significance was defined as p values < 0.05. All analyses were conducted using R version 4.0.3 software (R Foundation

Table 1 Baseline patient characteristics according to surgical prophylaxis exposure

	Overall *N* = 46 (100)	Standard prophylaxis *N* = 24 (52)	Targeted prophylaxis *N* = 22 (48)	*p*-value
Baseline characteristics				
Age, years	43 [33–52]	43 [35–50]	43 [31–55]	0.836
Male gender, *n* (%)	24 (52)	16 (67)	8 (36)	0.075
BMI, kg/m^2	21 [18–24]	21 [19–24]	20 [18–24]	0.812
Corticosteroids, *n* (%)	23 (50)	11 (46)	12 (55)	0.768
O_2 therapy, *n* (%)	38 (83)	21 (88)	17 (77)	0.451
Diabetes, *n* (%)	11 (24)	6 (25)	5 (23)	0.999
LAS	35 [34–39]	35 [34–39]	35 [33–39]	0.562
Oto score	3 [1–5]	3 [1–5]	2 [2–6]	0.827
Underlying diseases				
Septic[a], *n* (%)	30 (65)	15 (63)	15 (68)	0.763
Interstitial[b], *n* (%)	7 (15)	4 (17)	3 (14)	0.999
Obstructive[c], *n* (%)	8 (17)	4 (17)	4 (18)	0.999
Others[d], *n* (%)	1 (2)	1 (4)	0 (0)	-
Previous colonization				
Recipient-related MS GN bacteria	24 (52)	13 (58)	9 (45)	0.395
Recipient-related MDR GN bacteria	22 (48)	11 (42)	13 (55)	0.395
Donor-related GN bacteria[e]	13 (28)	8 (33)	5 (23)	0.521
Recipient-related viral colonization	2 (4)	0 (0)	2 (9)	0.476

Data are expressed as number and (percentage) or median and [interquartile range]. [a]Septic: cystic fibrosis, bronchiectasis; [b]Interstitial: idiopathic pulmonary fibrosis, allergic extrinsic alveolitis, non-specific interstitial pneumonia, fibrosing emphysema, lymphocytic interstitial pneumonia, respiratory bronchiolitis interstitial lung; [c]Obstructive: chronic obstructive pulmonary disease; [d]Others: idiopathic pulmonary hypertension, veno-occlusive disease, connective tissue disease, α1-antitrypsin deficiency, lymphangioleiomyomatosis, histiocytosis, sarcoidosis, graft versus host disease. *Abbreviations*: BMI, body mass index; *n*, number; O2, oxygen; LAS, lung allocation score; MS, multisensitive; GN, Gram-negative; MDR, multidrug-resistant; LT, lung transplant;

Table 2 Intraoperative characteristics according to surgical prophylaxis exposure

	Overall *N* = 46 (100)	Standard prophylaxis *N* = 24 (52)	Targeted prophylaxis *N* = 22 (48)	*p*-value
Intraoperative characteristics				
Time of LT, minutes	440 [348–490]	448 [368–490]	430 [339–486]	0.286
Time of graft ischemia, minutes	608 [506–755]	570 [439–683]	660 [523–784]	0.038
Blood transfusion, units	2 [1–3]	2 [1–4]	3 [1–3]	0.989
V-A ECMO pre-emptive	17 (37)	12 (50)	5 (23)	0.072
rescue	13 (28)	4 (17)	9 (41)	0.103
none	16 (35)	8 (34)	8 (36)	0.999
Surgical prophylaxis				
Carbapenems, *n* (%)	8 (17)	0 (0)	8 (36)	-
Ceftazidime-avibactam/ceftolozane-tazobactam ect, *n* (%)	10 (22)	0 (0)	14 (45)	-
β-lactam or III cephalosporins, *n* (%)	24 (52)	24 (100)	0 (0)	-
Colistin, fosfomycin, fluoroquinolones, *n* (%)	4 (9)	0 (0)	4 (18)[h]	-

Data are expressed as number and (percentage) or median and) or median and [interquartile range]. [h]: these antibiotics were used in combination with other antimicrobials. *Abbreviations*: LT, lung transplantation; V-A ECMO, venous-arterial extracorporeal membrane oxygenation

Table 3 Study outcomes according to surgical prophylaxis exposure

	Overall *N* = 46 (100)	Standard prophylaxis *N* = 24 (52)	Targeted prophylaxis *N* = 22 (48)	*p*-value
Primary outcomes	30 (65)	14 (58)	16 (73)	0.364
Secondary outcomes				
Infections by ESBL/MDR GN bacteria, *n* (%)	15 (33)	4 (17)[h]	11 (50)[h]	**0.027**
Colonizations by ESBL/MDR GN bacteria, *n* (%)	15 (33)	10 (42)	5 (23)	0.212
Other outcomes				
Infection by MS GN bacteria, *n* (%)	2(4)	1(4)	2(5)	0.999
Infection by GP bacteria, *n* (%)	6 (13)	2 (8)	4 (18)[l]	0.405
Invasive mechanical ventilation, hours	24 [20–59]	24 [19–64]	24 [20–59]	0.125
Re-tracheal intubation and/or tracheostomy, *n* (%)	10 (22)	2 (8)	8 (36)	**0.032**
Anastomotic complications, *n* (%)	4 (9)	2 (8)	2 (9)	0.999
30-day acute rejection[g], *n* (%)	11 (24)	8 (33)	3 (14)	0.171
ICU LOS, days	7 [5–17]	6 [3–14]	8 [6–23]	**0.002**
Hospital LOS, days	33 [30–45]	33 [30–38]	35 [31–50]	**0.039**
Hospital mortality, *n* (%)	3 (7)	0 (0)	3 (14)	0.101
ECMO post-surgery, *n* (%)	5 (11)	3 (13)	2 (9)	0.999
PGD at 72 h	1 [0–2]	1 [0–1]	1 [0–2]	0.286
Immunosuppressive therapy (cyclosporine (*ref*))[m]	30 (65)	13 (54)	17 (77)	0.129
Renal replacement therapy, *n* (%))	6 (13)	2 (8)	4 (19)	0.405

*Data are expressed as number and (percentage) or median and [interquartile range]. [h]: One patient treated with 'standard' prophylaxis and one patient with 'targeted' therapy, defined as 'infected' by MDR GN bacteria, had also a secondary colonization by different MDR GN bacteria; [l]: one recipient, infected by a MS GN bacteria, was also colonized by a MDR GN bacteria. [l]: one patients was colonized by postoperative MDR GN bacteria. [g]: rejection is defined according to International Society for heart and lung transplantation (ISHLT) criteria (i.e., A3-A4 and/or B2 grade at biopsy) [38]. [m]: The other LT recipients were treated with tacrolimus. *Abbreviations*: MDR, multidrug-resistant; MS, multisensitive; ICU, intensive care unit; LOS, length of stay; H, hospital; ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation; PGD, primary graft dysfunction; *n*, number

for Statistical Computing) and Prism version 5.0 software (GraphPad Software, Inc.).

Results

Overall, 181 patients underwent LT in our center between February 2016 and February 2023. Following eligibility criteria, 46 (25%) patients were included in the study (see study flow-chart in Fig. 1). Twenty-four (52%) pre-colonized recipients received 'standard' surgical prophylaxis, while 22 (48%) 'targeted' antibiotics. Baseline characteristics of both groups are described in Table 1. Twenty-four out of 46 (52%) enrolled patients were colonized by multisensitive GN bacteria and 22 (48%) by MDR GN bacteria. Most microorganisms were *Pseudomonas aeruginosa* and *Achromobacter xylosoxidans*, collected from respiratory samples (see full description of isolated bacteria in Table S1). Based on the available retrospective microbiological data from donors, 13 out of 46 (30%) donors tested positive on screening cultures, mostly from respiratory tract but never from blood stream (Table 1 and Table S1). β-lactam antibiotic or III cephalosporins were administered in all (100%) patients

undergoing 'standard' prophylaxis; carbapenems, ceftazidime-avibactam, ceftolozane-tazobactam, colistin, fosfomycin, and fluoroquinolones were exclusively used in the 'targeted' group (Table 2).

Prevalence of MDR GN bacteria after LT

The overall prevalence of postoperative MDR GN bacteria isolation was 65% (30 patients) within the first 30 days after surgery (Table 3). The prevalence of postoperative MDR GN bacteria isolation was 58% (14 out of 24 patients) in the 'standard' prophylaxis group and 73% (16 out of 22 patients) in patients receiving 'targeted' therapy ($p=0.364$) (Table 3; Fig. 2).

Considering only LT recipients with postoperative MDR GN bacteria, 11 out of 14 (79%) patients treated with 'standard' group and 12 out of 16 (75%) exposed to 'targeted' therapies reconfirmed the same preoperative GN pathogen ($p=0.999$). The most frequent MDR GN bacteria isolates were *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* from respiratory samples. More details on postoperative isolates are reported in Table S2.

Prevalence of MDR GN bacterial infections and colonizations

According to Sepsis-3 criteria [25] and CDC/NHSN Surveillance Definitions for Specific Types of Infections [38] 15 out of 46 (33%) recipients developed infections due to MDR GN bacteria: nine patients (60%) were diagnosed with pneumonia, one patient (13%) with bacteremia, and four (27%) reported infections from multiple sites. Most of these recipients (11 out of 15) were exposed to 'targeted' surgical prophylaxis and only 4 to 'standard' antibiotics ($p=0.027$).

In 15 out of 46 (33%) patients, colonizations due to MDR GN bacteria were observed: in 9 patients (60%) positive samples derived from the airways, in three patients (39%) from the digestive tract, in one patient (13%) from the urinary tract, and in two patients (26%) from multiple sites. No differences were found between 'standard' vs. 'targeted' prophylaxis ($p=0.217$) (Table 3).

As shown in Fig. 3, most (12 out of 15) colonizations and (9 out of 15) infections were recorded in recipients requiring LT due to septic end-stage lung diseases ($p=0.427$).

Other outcomes

Two (4%) recipients developed infections due to MS GN bacteria (p-value 0.999) and six (13%) patients due to GP bacteria ($p=0.405$), with no differences between different prophylaxis (Table 3). Compared to patients exposed to the 'standard' prophylaxis, patients belonging to the 'targeted' group more frequently required re-tracheal intubation and/or tracheostomy (36% vs. 8%, $p=0.032$), and recorded longer ICU and hospital stay (p-value 0.002 and 0.039, respectively) (Table 3).

Discussion

In 46 bilateral LT recipients with previous GN-colonizations and not exposed to mechanical ventilation, ECMO or hospitalization before LT, the prevalence of

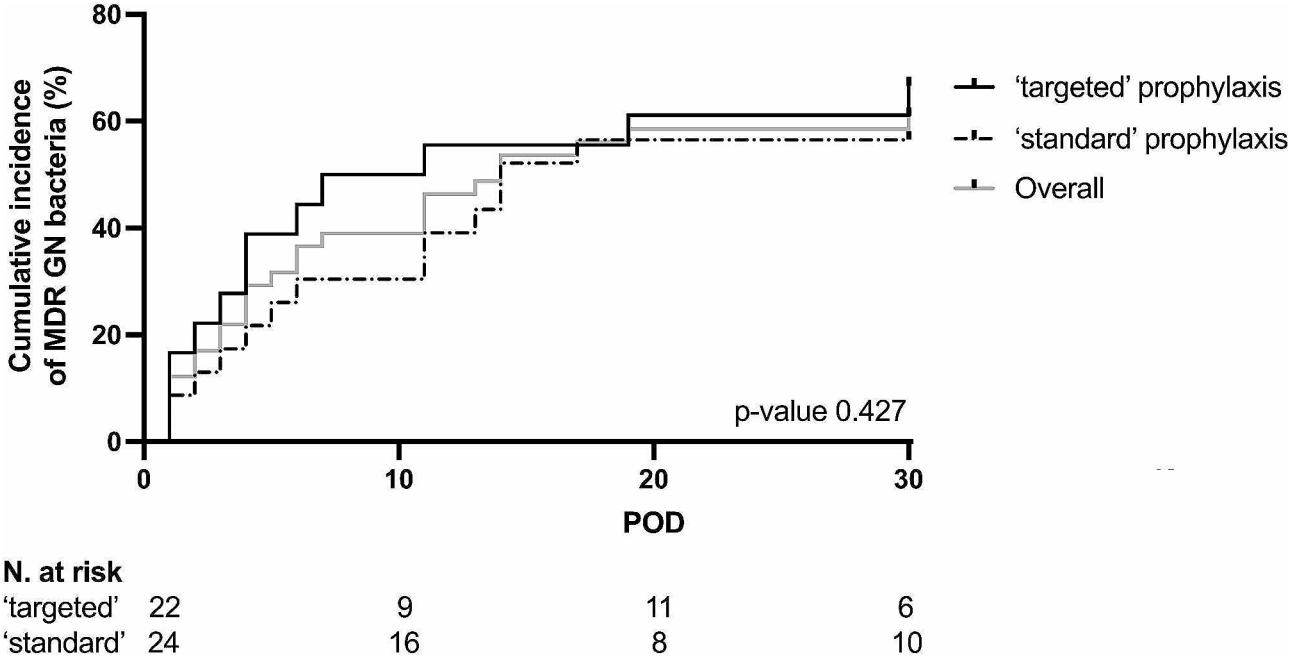

Fig. 2 Cumulative incidence of postoperative MDR GN bacteria isolation according to surgical prophylaxis exposure. *Abbreviations*: LT, lung transplant; POD, postoperative day; MS, multisensitive; MDR, multidrug resistant

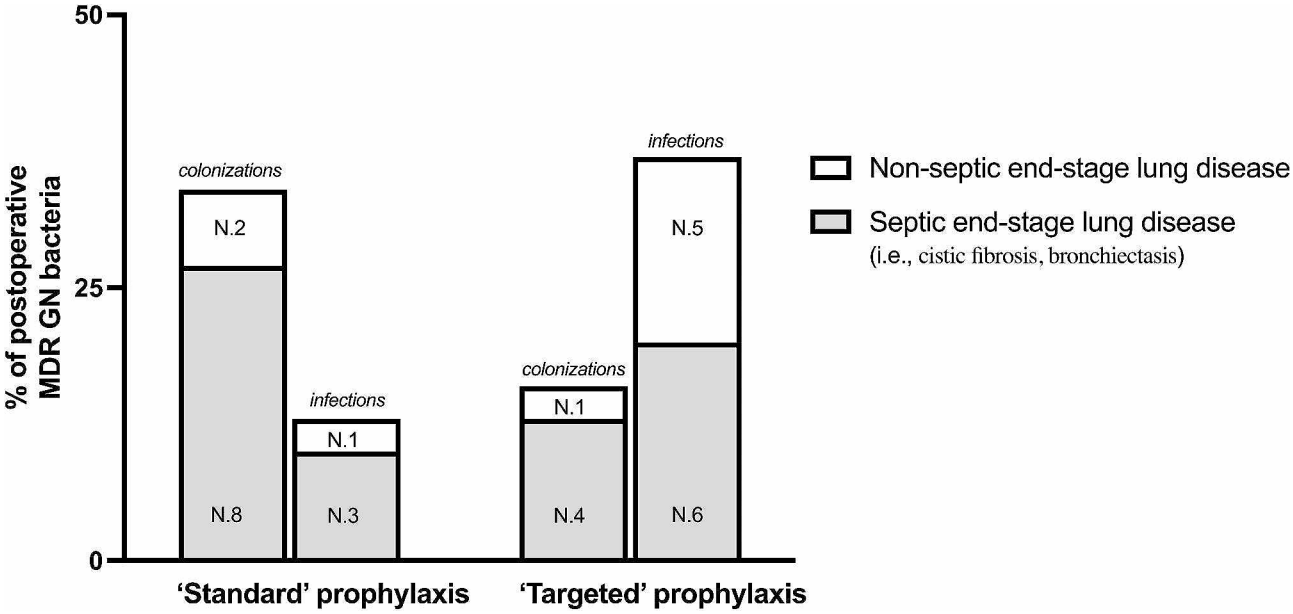

Fig. 3 Infections and colonizations after LT based on exposure to different surgical prophylaxis. *Abbreviations*: LT, lung transplant; ns, non significant; *N*, number. *p*-value 0.427

postoperative MDR GN bacteria was 65% within the first 30 days after surgery. In the whole cohort, 33% of patients developed postoperative colonizations and 33% of recipients infections due to MDR GN bacteria. Interestingly, in patients exposed to 'targeted' antimicrobial prophylaxis the prevalence of postoperative infections due to MDR GN bacteria and the rate of re-intubations were higher, as well the ICU and hospital LOS were longer, compared to those treated according to 'standard' surgical prophylaxis. Finally, the postoperative occurrence of preoperative GN pathogens was similar between groups.

To the best of our knowledge, this is the first study exclusively including LT adult recipients pre-colonized by GN bacteria and describing the perioperative MDR GN bacterial epidemiology in this 'specific' patient population. Due to the remarkable worldwide increase of highly resistant pathogens, more data on the potential benefits of 'personalized' surgical antimicrobial prophylaxis are required. However, few studies have been published on this topic so far [7, 6, 24, 39–41].

According to the most recent literature, the rate of preoperative GN colonization in LT recipients is still unclear [6, 7, 24, 40]. Recent findings suggest that the presence of preoperative MDR bacteria ranged from 1.1% to up to >50% in recipients with cystic fibrosis [7, 20]. Our findings are in keeping with previous studies suggesting that previous antimicrobial treatments are key to the occurrence of highly resistant bacteria isolations after LT [6, 24, 40].

With regards to the occurrence of postoperative infection due to MDR GN bacteria, our prevalence of 33% is in line with previous investigations [7, 14]. However, these studies did not exclusively enroll pre-colonized LT recipients, but patients receiving solid organ transplants with or without pre-existing bacterial isolations [6, 14], thus highlighting that previous recipient-related colonizations are not necessarily associated with a greater risk of infection [6, 14].

We reported a similar prevalence between postoperative colonizations (33%) and infections (33%) due to MDR GN bacteria. Noteworthy, we observed that the exposure to a 'targeted' antimicrobial surgical prophylaxis was associated with increased risk of postoperative infections by highly resistant bacteria, especially in recipients needing LT due to septic end-stage lung diseases (i.e., cystic fibrosis or bronchiectasis). This finding is in keeping with Boscolo et al. and Paglicci et al., who reported that the use of 'standard' antibiotic prophylaxis, when compared to broad-spectrum antibiotic regimens, reduced the incidence of highly resistant bacteria infection after LT [6, 7]. Moreover, the 'targeted' prophylaxis did not prevent the occurrence of the preoperative GN bacteria during the first month after surgery [7, 14].

Our preliminary findings may suggest that antimicrobial surgical prophylaxis titrated on preoperative GN bacteria colonizations in LT recipients, at low-risk of postoperative complications, might promote the selection of resistant bacteria, increasing the risk of postoperative infections, and affect patient outcomes. The last updated guidelines from the American Society of Transplantation and European Society of Clinical Microbiology and Infectious Diseases confirmed that heightened infection control and antimicrobial stewardship initiatives are needed to prevent these 'difficult-to-treat'

infections, curtail their transmission, and limit the evolution of MDR GN pathogens. Despite these recommendations, no clear information has been described about the use of 'personalized' perioperative prophylaxis but a strong recommendation has been reported about the sparing of carbapenems and other antibiotics for the risk to select resistant microorganisms [21]. The International consensus recommendations for anesthetic and intensive care management of lung transplantation, released in 2022 and keeping in line with our findings, confirmed that in uncomplicated LT recipients with low risk for donor and recipient-derived infection, as those patients enrolled in our study, a short antibacterial prophylaxis, primarily aimed at preventing surgical site infections, should be administered (*strong consensus*). Noteworthy, in case of positive cultures, postoperative antimicrobial treatment should be modified according to the isolated microorganism and the risk of postoperative infections [22]. On the contrary, the last Spanish guidelines, albeit with *weak evidence*, are in favor of personalized antibiotic prophylaxis based on the pre-existing colonization. However, the same authors underlined the importance to balance the risk of infection against the risk of developing adverse effects to the antibiotics and/or carbapenem-resistance [23].

Our study has some limitations. First, it is a retrospective monocentric observational study which needs to be confirmed by well-designed randomized clinical trials without biases related to a 'non-standardized' antimicrobial prescription. The retrospective nature of the study did not allow to investigate the reasons of targeted prophylaxis, potentially related to the patient's clinical history and baseline characteristics at the time of transplant. Second, microbiological data and morbidity rate were only investigated within 30 days after LT and not later. However, many studies have found a greater occurrence of MDR bacteria within the first month following surgery [5, 6]. Third, we did not report in our study cohort, frequent occurrence of viral infection or precolonized, well-known risk factors of morbidity in LT recipients, as suggested by literature data [42].

Moreover, the small sample size did not allow us to perform any multivariable regression analysis or to apply a Propensity Score methodology for minimizing potential differences between sub-groups. Therefore, our results barely suggest an association between the choice of antimicrobial surgical prophylaxis and the analyzed outcomes in LT patients, without excluding potential selection biase. Lastly, we excluded recipients with pre-colonizations due to GP bacteria, as their impact seems to be declining in solid organ transplant recipients [18, 34].

Conclusions

In our cohort of 46 bilateral LT recipients with preoperative GN bacteria, the occurrence of postoperative isolations of MDR GN bacteria was frequent (65%) but not necessarily associated with a high risk of postoperative infection. In fact, a prophylactic antibiotic approach tailored to preoperative colonizations was mostly associated with an increased prevalence of postoperative MDR GN bacterial infections and worse short- and mid-term clinical outcomes, as compared to a 'standard' prophylaxis.

Abbreviations

LT	Lung transplant
IMV	Invasive mechanical ventilation
ECMO	Extracorporeal membrane oxygenation
GP	Gram-positive

Supplementary Information

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Supplementary Material 1

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Author contributions

Conceptualization, S.C., A.B., P.N., F.R., A.C., A.D., S.M. and M.B.; methodology, A.B., T.P., N.S.; formal analysis, A.B., T.P., S.N.; data curation, A.P., L.M., A.AS.T., I.C., F.M., E.R., G.R., S.M., M.M., F.M., S.C.; writing original draft preparation, A.B., M.B., S.C., T.P., N.S.; writing review and editing, P.N., L.M., A.P., S.M., M.M., A.D.; supervision, A.C., A.D., F.R., P.N., A.B. All authors have read and agreed to the published version of the manuscript.

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Data availability

"The datasets used and/or analysed during the current study available from the corresponding author on reasonable request".

Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

The study was approved by the Institutional Ethic Committee of Padua University Hospital (reference number 0025364) and was conducted in accordance with the principles of Good Clinical Practice and according to the Declaration of Helsinki. Written informed consent was obtained from all subjects and/or their legal representatives. The article was written in accordance with the "strengthening the reporting of observational studies in epidemiology-STROBE" checklist (Table S3).

Consent for pubblication

Not applicable.

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References

1. Khush KK, Cherikh WS, Chambers DC, Harhay MO, Hayes D, Hsich E. etal.The international thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: thirty-sixth adult heart transplantation report– 2019; focus theme: Donor and recipient size match.J Heart Lung Transplant Off Publ Int Soc Heart Transplant.2019;38*(10)*:1056–66.
2. Nosotti M, Tarsia P, Morlacchi LC. Infections after lung transplantation. J Thorac Dis. 2018;10(6):3849–68.
3. Congedi S, Navalesi P, Boscolo A. Multidrug-resistant organisms in lung transplant: a narrative review.Curr Opin Organ Transplant.2023.
4. Lanini S, Costa AN, Puro V, Procaccio F, Grossi PA, Vespasiano F. etal.Incidence of carbapenem-resistant gram negatives in Italian transplant recipients: a nationwide surveillance study.PloS One.2015;10*(4)*:e0123706.
5. Tebano G, Geneve C, Tanaka S, Grall N, Atchade E, Augustin P. Epidemiology and risk factors of multidrug-resistant bacteria in respiratory samples after lung transplantation. Transpl Infect Dis off J Transpl Soc. 2016;18(1):22–30.
6. Boscolo A, Sella N, Pettenuzzo T, De Cassai A, Crociani S, Schiavolin C. etal. Multidrug-resistant and extended-spectrum β-Lactamase gram-negative Bacteria in bilateral lung transplant recipients: incidence, risk factors, and In-Hospital mortality.Chest. 2022;162*(6)*:1255–64.
7. Paglicci L, Borgo V, Lanzarone N, Fabbiani M, Cassol C, Cusi MG. etal.Incidence and risk factors for respiratory tract bacterial colonization and infection in lung transplant recipients.Eur J Clin Microbiol Infect Dis Off Publ Eur Soc Clin Microbiol.2021;40*(6)*:1271–82.
8. Boscolo A, Dell'Amore A, Pettenuzzo T, Sella N, De Cassai A, Pistollato E. etal. The impact of New treatments on short- and MID-Term outcomes in bilateral lung transplant: a propensity score study.J Clin Med. 2022;11*(19)*:5859.
9. Chung PA, Dilling DF. Immunosuppressive strategies in lung transplantation. Ann Transl Med. 2020;8*(6)*:409.
10. Ivulich S, Westall G, Dooley M, Snell G. The evolution of lung transplant immunosuppression.Drugs.2018;78*(10)*:965–82.
11. Antimicrobial resistance [Internet]. [cited2023Apr6].Availablefrom:https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance.
12. Burguete SR, Maselli DJ, Fernandez JF, Levine SM. Lung transplant infection. Respirol Carlton Vic.2013;18*(1)*:22–38.
13. Fishman JA. Infection in Organ Transplantation.Am J Transplant Off J Am Soc Transplant Am Soc Transpl Surg.2017;17*(4)*:856–79.
14. Remund KF, Best M, Egan JJ. Infections relevant to lung transplantation.Proc Am Thorac Soc2009;*6(1)*:94–100.
15. Coiffard B, Prud'Homme E, Hraiech S, Cassir N, Le Pavec J, Kessler R. etal. Worldwide clinical practices in perioperative antibiotic therapy for lung transplantation.BMC Pulm Med.2020;20*(1)*:109.
16. Oriol I, Sabé N, Simonetti AF, Lladó L, Manonelles A, González J. etal. Changing trends in the etiology, treatment and outcomes of bloodstream infection occurring in the first year after solid organ transplantation: a single-centre prospective cohort study.Transpl Int Off J Eur Soc Organ Transplant.2017;30*(9)*:903–13.
17. Zenati M, Dowling RD, Dummer JS, Paradis IL, Arena VC, Armitage JM. etal. Influence of the donor lung on development of early infections in lung transplant recipients.J Heart Transplant. 1990;9*(5)*:502–8;discussion 508–509.
18. Bartoletti M, Giannella M, Tedeschi S, Viale P. Multidrug-resistant bacterial infections in solid organ transplant candidates and recipients. Infect Dis Clin North Am. 2018;32(3):551–80.
19. Di Nardo M, Tikkanen J, Husain S, Singer LG, Cypel M, Ferguson ND. etal. Postoperative management of lung transplant recipients in the Intensive Care Unit.Anesthesiology.2022;136*(3)*:482–99.
20. van Duin D, van Delden C. Multidrug-resistant gram-negative Bacteria infections in solid organ transplantation.Am J Transplant.2013;13:31–41.
21. Pouch SM, Patel G, AST Infectious Diseases Community of Practice. Multidrug-resistant Gram-negative bacterial infections in solid organ transplant recipients-guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant.2019;33*(9)*:e13594.
22. Marczin N, de Waal EEC, Hopkins PMA, Mulligan MS, Simon A, Shaw AD. etal. International consensus recommendations for anesthetic and intensive care management of lung transplantation. An EACTAIC, SCA, ISHLT, ESOT, ESTS, and AST approved document.J Heart Lung Transplant Off Publ Int Soc Heart Transplant. 2021;40*(11)*:1327–48.
23. Aguado JM, Silva JT, Fernández-Ruiz M, Cordero E, Fortún J, Gudiol C. etal. Management of multidrug resistant gram-negative bacilli infections in solid organ transplant recipients: SET/GESITRA-SEIMC/REIPI recommendations. Transplant Rev Orlando Fla.2018;32*(1)*:36–57.
24. Cervera C, van Delden C, Gavaldà J, Welte T, Akova M, Carratalà J. etal. Multidrug-resistant bacteria in solid organ transplant recipients. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis.2014;20 Suppl 7:49–73.
25. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M. The Third International Consensus definitions for Sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):801–10.
26. Cuschieri S. The STROBE guidelines. Saudi J Anaesth.2019;13*(*Suppl 1*)*:S31–4.
27. eucast. Clinicalbreakpointsanddosingofantibiotics[Internet].[cited2023Apr5]. Availablefrom:https://www.eucast.org/clinical_breakpoints.
28. Timsit JF, Huntington JA, Wunderink RG, Shime N, Kollef MH, Kivistik Ü. etal. Ceftolozane/tazobactam versus meropenem in patients with ventilated hospital-acquired bacterial pneumonia: subset analysis of the ASPECT-NP randomized, controlled phase 3 trial.Crit Care Lond Engl.2021;*25(1)*:290.
29. Klompas M, Branson R, Cawcutt K, Crist M, Eichenwald EC, Greene LR. etal. Strategies to prevent ventilator-associated pneumonia, ventilator-associated events, and nonventilator hospital-acquired pneumonia in acute-care hospitals: 2022 update.Infect Control Hosp Epidemiol.2022;43*(6)*:687–713.
30. Mahajan AK, Folch E, Khandhar SJ, Channick CL, Santacruz JF, Mehta AC. The diagnosis and management of Airway complications following lung transplantation. Chest. 2017;152(3):627–38.
31. Tiseo G, Brigante G, Giacobbe DR, Maraolo AE, Gona F, Falcone M. etal.Diagnosis and management of infections caused by multidrug-resistant bacteria: guideline endorsed by the Italian Society of Infection and Tropical Diseases (SIMIT), the Italian society of anti-infective therapy (SITA), the Italian Group for Antimicrobial Stewardship (GISA), the Italian Association of Clinical microbiologists (AMCLI) and the Italian Society of Microbiology (SIM).Int J Antimicrob Agents.2022;60*(2)*:106611.
32. Martin-Loeches I, Torres A, Nagavci B, Aliberti S, Antonelli M, Bassetti M. etal.ERS/ESICM/ESCMID/ALAT guidelines for the management of severe community-acquired pneumonia.Intensive Care Med.2023;1–18.
33. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG. etal.Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance.Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis.2012;18*(3)*:268–81.
34. Rossolini GM, Bochenska M, Fumagalli L, Dowzicky M. Trends of major antimicrobial resistance phenotypes in enterobacterales and gram-negative non-fermenters from ATLAS and EARS-net surveillance systems: Italian vs. European and global data, 2008–2018.Diagn Microbiol Infect Dis. 2021;101*(4)*:115512.
35. Paul M, Carrara E, Retamar P. etal.European Society of Clinical Microbiology and Infectious diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine).Clin Microbiol Infect.2022;28*(4)*:521–47.
36. Magiorakos A-P, Srinivasan A, Carey RB. etal.Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance.Clin Microbiol Infect. 2012;18*(3)*:268–81.
37. Nabal Diaz SG, Robles OA, Moya JMGL. New definitions of susceptibility categories EUCAST 2019: clinic application.Rev Esp Quimioter.2022;35*(3)*:84–8.
38. (https://www.cdc.gov/nhsn/pdfs/pscmanual/17pscnosinfdef_current.pdf).
39. Avtaar Singh SS, Banner NR, Rushton S, Simon AR, Berry C, Al-Attar N. ISHLT primary graft dysfunction incidence, risk factors, and outcome: a UK National Study.Transplantation.2019;103*(2)*:336–43.
40. Silva JT, Fernández-Ruiz M, Aguado JM. Multidrug-resistant Gram-negative infection in solid organ transplant recipients: implications for outcome and treatment.Curr Opin Infect Dis.2018;31*(6)*:499–505.
41. Jin M, Zeng L, Zhang W, Deng X, Li J, Zhang W. Clinical features of multidrug-resistant organism infections in early postoperative solid organ transplantation in a single center. Ann Palliat Med. 2021;10(4):4555–62.
42. Munting A, Manuel O. Viral infections in lung transplantation.J Thorac Dis.2021;13(11):6673–94.https://doi.org/10.21037/jtd-2021-24.

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