







# Hydrogen Peroxide Vapor Disinfection in Liver Transplantation: Effects on Multidrug-Resistant Organism Colonization and Recipient Outcomes

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## ABSTRACT

**Introduction:** The escalation of multidrug-resistant organism (MDRO) infections post-liver transplantation (LT) poses significant risks, with MDRO colonization amplifying infection susceptibility. Environmental disinfection is crucial in curbing healthcare-associated infections (HAI). Hydrogen peroxide vapor (HPV) technology offers promise, yet its impact on MDRO infections and patient outcomes remains unclear. **Methods:** A cohort study enrolled 58 deceased adult LT recipients, comparing outcomes before and after routine HPV implementation. HPV disinfection followed terminal cleaning in surgical rooms and intensive care unit (ICU) boxes. Pathogen data included pre-transplant and post-discharge MDRO colonization. Clinical data covered recipient characteristics, disease severity, and donor-recipient relationships. Statistical analyses assessed associations and outcomes. **Results:** Twenty-seven patients were in the before-HPV group, 24 in the after-HPV group. Demographic and clinical characteristics were comparable between groups. HPV implementation significantly increased the likelihood of negative control swabs (odds ratio 2.33). *Klebsiella pneumoniae* carbapenemase was the most frequent pathogen, with surgical site infections being the primary site. Patients with negative swabs had shorter hospital stays (mean difference 10.54 days), notably diverging around the 8th day of hospitalization. HAI frequency and 90-day mortality were significantly lower in patients with negative swabs. **Conclusion:** HPV technology effectively reduced MDRO colonization in LT recipients. Negative swabs correlated with shorter hospital stays and lower HAI frequency, impacting 90-day mortality positively. Despite challenges in HPV implementation, its efficacy in reducing MDRO colonization suggests a valuable tool in infection control strategies for vulnerable populations like LT recipients.

**Descriptors:** Liver Transplantation; Multi-Drug-Resistant Organisms; Health Care-Associated Infections; Environmental Contamination.

*Desinfecção por Vapor de Peróxido de Hidrogênio no Transplante de Fígado: Efeitos na Colonização de Organismos Multirresistentes e nos Resultados do Receptor*

## RESUMO

**Introdução:** A escalada das infecções por organismos multirresistentes (MR) pós-transplante de fígado (TF) representa riscos significativos, com a colonização por MR amplificando a suscetibilidade à infecção. A desinfecção ambiental é crucial para conter as infecções associadas à assistência à saúde (IRAS). A tecnologia de vapor de peróxido de hidrogênio (VPH) oferece promessas, mas seu impacto nas infecções por MR e nos resultados dos pacientes ainda não está claro. **Métodos:** Um estudo de coorte incluiu 58 receptores de TF adultos, comparando os resultados antes e depois da implementação rotineira do VPH. A desinfecção por VPH seguiu a limpeza terminal em salas cirúrgicas e boxes de unidade de terapia intensiva. Os dados dos patógenos incluíram colonização por MR no pré- e pós-transplante. Os dados clínicos abrangeram características dos receptores, gravidade da doença e características do binômio doador-receptor. As análises estatísticas avaliaram associações e resultados.

**Resultados:** Vinte e sete pacientes estavam no grupo antes do VPH e 24 no grupo após o VPH. As características demográficas e clínicas foram comparáveis entre os grupos. A implementação do VPH aumentou significativamente a probabilidade de resultados negativos nos *swabs* de controle (razão de chances 2,33). *Klebsiella pneumoniae* carbapenemase foi o patógeno mais frequente, com infecções do sítio cirúrgico sendo o local primário mais comum. Pacientes com *swabs* negativos tiveram internações hospitalares mais curtas (diferença média de 10,54 dias), divergindo notadamente por volta do 8º dia de internação. A frequência de IRAS e a mortalidade em 90 dias foram significativamente menores em pacientes com *swabs* negativos. **Conclusão:** A tecnologia de VPH reduziu efetivamente a colonização por MR em receptores de TF. *Swabs* negativos se correlacionaram com internações hospitalares mais curtas e menor frequência de IRAS, impactando positivamente a mortalidade em 90 dias. Apesar dos desafios na implementação do VPH, sua eficácia na redução da colonização por MR sugere uma ferramenta valiosa nas estratégias de controle de infecções para populações vulneráveis como receptores de TF.

**Descritores:** Transplante de Fígado; Organismos Multirresistentes; Infecções Associadas aos Cuidados de Saúde; Contaminação Ambiental.

## INTRODUCTION

The frequency of post-transplant infections in liver transplantation (LT) attributed to multidrug-resistant organisms (MDRO) has escalated.<sup>1</sup> MDRO colonization in this vulnerable population amplifies the risk of infection,<sup>2</sup> which is associated with greater graft loss, longer hospital stays, higher healthcare costs, and increased mortality after transplant.<sup>3</sup>

The significance of infection prevention and antibiotic stewardship in curbing the rise and spread of MDRO is widely acknowledged. Moreover, the role of environmental disinfection in the transmission of healthcare-associated infections (HAI) is within this framework.<sup>4,5</sup>

Environmental contamination accounts for an estimated 10 to 30% of MDRO acquisitions in intensive care units (ICUs),<sup>6</sup> though these rates vary significantly across hospitals and regions. This variability reflects broader structural challenges, particularly in low- and middle-income countries,<sup>7</sup> where high MDRO mortality rates are driven by systemic issues such as fragmented healthcare systems, overcrowded facilities, workforce shortages, limited infection control personnel, underdeveloped microbiological services, and restricted access to essential antibiotics.<sup>8</sup> These disparities create uneven MDRO acquisition rates, complicating efforts to establish uniform prevention and control strategies across healthcare environments.

Non-touch technologies for whole-room disinfection such as H<sub>2</sub>O<sub>2</sub> vapor (HPV) and automated germicidal ultraviolet irradiation can enhance the quality of terminal disinfection in patient rooms,<sup>9</sup> with HPV achieving the highest microbial reduction in vitro.<sup>10</sup> The true question, however, is whether the effectiveness of non-manual disinfection approaches in reducing environmental contamination – compared to conventional disinfection – significantly lowers MDRO infections or modifies survival rates. The current literature provides limited evidence on these clinical outcomes,<sup>11</sup> which is a gap that the presented study aims to address.

Given the burden of MDRO colonization and resultant HAIs in LT, the primary objective of the study was to determine the efficacy of HPV technology, employed after terminal cleaning, in reducing the percentage of rectal colonization by MDRO in patients undergoing LT. Secondary objectives included analyzing the impact of rectal colonization on HAI and patient survival.

## METHODS

The study enrolled 58 deceased adult liver transplant recipients in a cohort study design. Twenty-nine transplants performed after the routine implementation of the HPV system from Nocotech Concept®, were compared with the last 29 transplants conducted before the use of HPV. The study spanned 19 months (April 2022 to November 2023).

Daily routine terminal cleaning, followed by HPV disinfection, was conducted in the surgical room where the transplant took place. Similarly, routine terminal cleaning followed by HPV was performed in the ICU box just before the patient's arrival after surgery. The process of HPV disinfection involved deploying the aerial surface biodesinfection device, followed by dry mist spraying of a stabilized 12% hydrogen peroxide solution with silver from Nocotech Concept® for 5 minutes. The time of mist application was adjusted based on the volume of the room. The dry mist naturally dissipates without leaving any residue or causing surface corrosion, including on electronic and mechanical surfaces. No wiping or ventilation was necessary. Throughout the operation of the machine and the contact time (60 minutes), the ICU/surgical room

remained sealed and uninhabited. Culture dishes were utilized to detect the presence of bacteria, and test strips were employed for semi-quantitative detection of hydrogen peroxide during the pre-implementation product evaluation to assess environmental cleanliness. Routine environmental sampling was not conducted during the study period.

Routine terminal cleaning involves the sequential use of hospital detergent followed by hospital disinfectant, containing polyhexamethylene biguanide (PHMB) and quaternary ammonium compounds. Within the ICU, daily cleaning duties are executed collaboratively by both the hygiene and cleaning team (responsible for bins and floor sanitation) and the nursing team, ensuring comprehensive cleaning and disinfection of various surfaces, including the bed, bedside table, equipment, monitors, and pumps. Moreover, every 7 days during a patient's ICU stay, temporary relocation is arranged to facilitate thorough terminal cleaning of the ICU enclosure.

Pathogen data collected included MDRO rectal colonization (perirectal swabs) before LT and after discharge from the ICU, or during any significant clinical change during ICU recovery. Acquisitions were defined as the identification of an MDRO after  $\geq 48$  hours of admission in a patient with no known prior history of that organism.<sup>12</sup> Patients with positive rectal swabs before transplantation were excluded. Rectal swabs were analyzed using MALDI-TOF mass spectrometry for identification of microorganisms. Antimicrobial susceptibility testing was conducted through automated broth microdilution techniques, following the Brazilian Committee on Antimicrobial Susceptibility Testing (BrCAST) standards for antibiograms.<sup>13</sup>

Clinical data collected included recipient variables such as age, sex, primary diagnosis, body mass index (BMI), creatinine clearance as calculated by the modification of diet in renal disease (MDRD-6) and Cockcroft-Gault equation (Cockcroft), muscle waist,<sup>14</sup> presence of diabetes, medical condition at the time of transplantation (whether they were in the home, medical ward, or ICU), diagnosis of acute-on-chronic liver failure (ACLF) (European Association for the Study of the Liver definition), and previous antibiotic use defined as exposure to broad-spectrum Gram-negative antibiotics prior to transplantation. The antibiotic regimen used in surgical prophylaxis was recorded.

Variables used to estimate disease severity included the Child-Turcotte-Pugh score (CHILD), Model for End-Stage Liver Disease with sodium correction and its 3.0 version (MELD; MED 3.0), Freiburg index of post-TIPS survival (FIPS), MELD-PSOAS,<sup>14</sup> and the preallocation score to predict survival following LT (P-SOFT). Variables intended to analyze donor-recipient relationships included survival outcomes following LT score (SOFT), balance risk of score (BAR), donor age\*recipient MELD (DMELD), and ID2EAL-DR. Cold ischemia time and graft function<sup>15</sup> were analyzed as potential risk factors for MDRO colonization. Hand hygiene compliance was monitored by direct observation.<sup>16</sup> Patient survival at 90 days, HAI, and duration of hospital stay were recorded as outcome variables.

Digital data storage, management, and statistical analyses were performed using EpiInfo software.<sup>17</sup> In addition to employing statistical software for analyses, interactions, and discussions, a complementary validation process was conducted utilizing artificial intelligence via the Julius platform<sup>18</sup> to cross-verify and enhance the accuracy of the findings. To assess significant associations between two categorical variables, the chi-square test for independence was used. For continuous variables with a normal distribution, a t-test was executed, while for those that did not follow a normal distribution, the Mann-Whitney *U* test was employed. To explore the association between the status of the control swab and the cleaning method, the odds ratio (OR) was calculated using a  $2 \times 2$  contingency table and sought a quantitative measure of the strength of their association was sought, followed by the determination of the confidence interval (CI) and p-value. Bootstrap methods were used to estimate the distribution of a statistic (e.g., mean, median) and to construct CIs for the length of hospital stay.

The study protocol was designed in accordance with the ethical guidelines of the 1975 Declaration of Helsinki. The present study complies with the guidelines endorsed by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative.<sup>11</sup> Although not interventional in nature, the study was reviewed by the ethical committee through Plataforma Brasil under CAAE 65198822.6.0000.0020.

## RESULTS

Out of the 58 LTs included in the study, two patients in the group before HPV use (bHPV) and five in the group after HPV use (aHPV) were excluded due to positive screening results from perirectal swabs for MDRO. This resulted in 27 patients in the bHPV group and 24 in the aHPV group. The analyses did not have missing data. Demographic, clinical characteristics, and the etiology of liver disease were similar between the groups and are presented in Table 1.

**Table 1.** Demographic and clinical characteristics.

Characteristics	bHPV group (n = 27)	aHPV group (n = 24)	p-value
Patient age	48.72 ± 14.45	55.75 ± 8.12	0.058
Male sex	72%	70%	1.00
BMI	26.56 ± 5.43	24.55 ± 3.79	0.168
Muscle waist	17.66 ± 4.37	16.86 ± 5.09	0.574
MDRD6	70.98 ± 29.04	62.71 ± 32.03	0.369
Cockcroft	99.04 ± 49.53	83.85 ± 39.38	0.270
Diabetes	20%	10%	0.612
<b>Primary diagnosis</b>			
Alcohol	52%	55%	0.449
Cryptogenic	16%	25%	
MASLD	12%	5%	
Acute liver failure	8%	-	
Other	16%	15%	
<b>Medical condition</b>			
Home	76%	70%	0.72
Medical ward	4%	10%	
ICU	20%	20%	
ACLF	16%	15%	

Source: Elaborated by the authors. Cockcroft = creatinine clearance by Cockcroft-Gault equation; Muscle waist = transverse psoas muscle thickness standardized by height; MASLD = metabolic dysfunction associated liver disease.

The mathematical indices employed for assessing disease severity and analyzing donor-recipient relationships were compared (as shown in Table 2), indicating no significant differences between the groups.

**Table 2.** Disease severity and donor-recipient relationship.

Child	bHPV group (n = 27)	aHPV group (n = 24)	p-value
A	-	5%	0.288
B	36%	50%	
C	64%	45%	
MELD	21.84 ± 8.67	20.1 ± 8.24	0.498
MELD 3.0	21.2 ± 8.7	20.3 ± 8.4	0.729
FIPS	0.48 ± 1.33	0.49 ± 1.24	0.985
P-SOFT	7.48 ± 4.38	8.75 ± 4.91	0.365
MELDPSOAS	5.10 ± 1.95	4.86 ± 1.52	0.647
BAR	8.6 ± 4.22	7.7 ± 4.10	0.475
DMELD	1024.64 ± 402.98	1032.95 ± 526.02	0.952
SOFT	10.12 ± 4.53	10.85 ± 4.29	0.585
ID2ALDR	1.26 ± 0.29	1.29 ± 0.40	0.765

Source: Elaborated by the authors. ID2EALDR = ID2EAL score balanced with recipient characteristics; MELDPSOAS = modified MELD for sarcopenia.

The previous use of antibiotics, reported by 40% in the bHPV group and 65% in the aHPV group, did not influence the results of the control swab ( $p = 0.171$ ). The antibiotic regimen used in surgical prophylaxis did not differ between groups ( $p = 0.79$ ), with ampicillin-sulbactam and cefotaxime being used 92% of the time in the bHPV group and 85% in the aHPV group.

Hand hygiene compliance slightly improved after the implementation of HPV (aHPV group), rising to 71.19% from 70% before implementation (bHPV group). However, this difference was not statistically significant ( $p = 0.5845$ ).

Cold ischemia time was found to be significantly different between the two groups ( $7.83 \pm 1.38$  in bHPV vs.  $6.83 \pm 1.53$  in aHPV,  $p = 0.026$ ). The incidence of delayed graft function (DGF) was 12% in the bHPV group and 20% in the aHPV group. Additionally, the percentage of patients with normal graft function was 88% in the bHPV group and 80% in the aHPV group. The  $p$ -value obtained from comparing DGF and normal graft function was 0.747.

The frequency of a negative control swab increased from 34.48% in the bHPV group to 55.17% in the aHPV group, with a *p*-value of 0.0469.

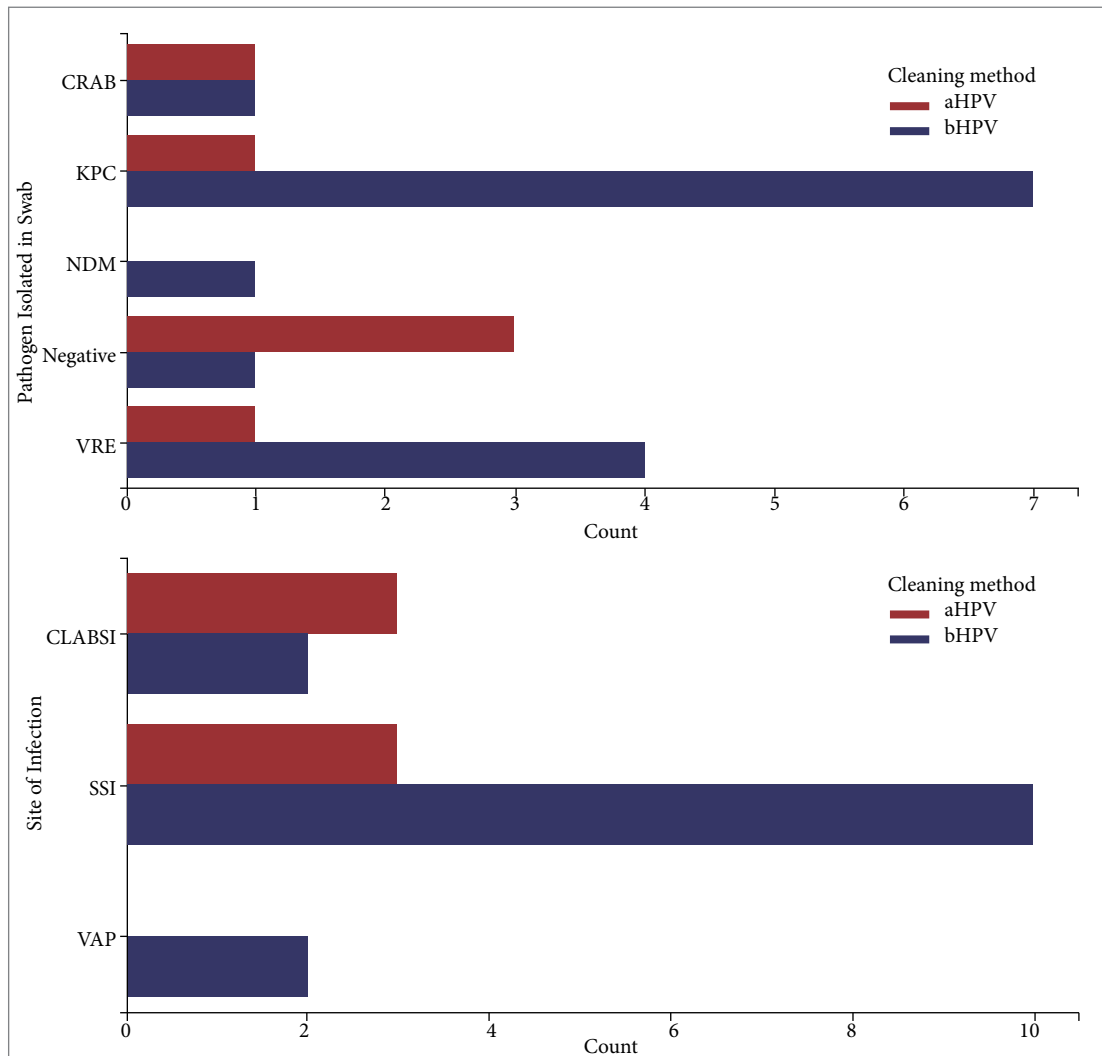
Given the findings of groups with similar characteristics and the study design, the OR approach was employed to compare the frequency of a negative outcome of the control swab with the use of the HPV system. The odds and CI are presented in Table 3.

**Table 3.** Odds and CI for the association between HPV and a negative result of the control swab.

Cleaning method	Odds of negative result	95%CI
After HPV	2.33	1.0058-12.1792
Before HPV	0.67	

Source: Elaborated by the authors.

*Klebsiella pneumoniae* carbapenemase (KPC) was the most frequent pathogen, accounting for 40% of the cases, while surgical site infection (SSI) was the most common site of infection, representing 65% of the cases. Neither the differences in isolated pathogens (*p* = 0.2067) nor the site of infection (*p* = 0.2077) between the groups achieved statistical significance; nevertheless, for schematic viewing, they are depicted in Fig. 1.



Source: Elaborated by the authors. CLABSI = central line-associated bloodstream Infection; CRAB = carbapenem-resistant *Acinetobacter baumannii*; NDM = New Delhi metallo-beta-lactamase-producing carbapenem-resistant enterobacterales; VAP = ventilator-associated pneumonia; VRE = vancomycin-resistant enterococci.

**Figure 1.** Pathogens isolated and site of infection before and after HPV cleaning.

The impact of the swab statuses on the length of hospital stays, analyzed using time-to-event analysis (whether discharge or death) employing Bootstrap methods, is presented in Table 4.

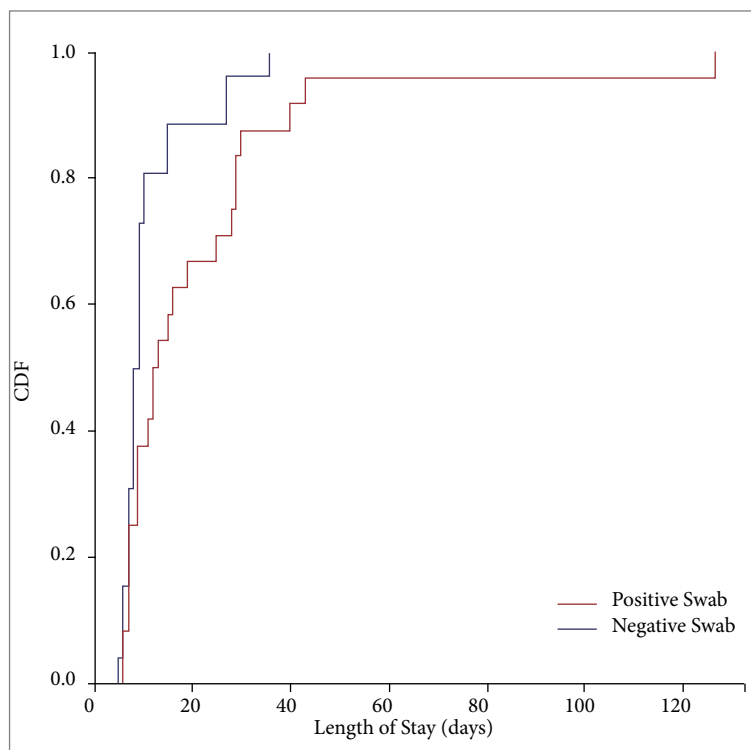
**Table 4.** Distribution of a statistic and CI by Bootstrap method.

Swab Result (Positive/Negative)	Hospital Stay Duration (Days, Confidence Interval)
Bootstrap CI – Positive swab (days)	13.67 to 33.17
Bootstrap CI – Negative swab (days)	8.46 to 14.08
Mean difference in length of stay (days)	10.54
Adjusted CI for difference in means (days)	1.97 to 22.43

Source: Elaborated by the authors.

The difference in length of stay between the two groups was significant. The Mann-Whitney  $U$  test resulted in a  $U$  statistic of 430.0 and a  $p$ -value of approximately 0.0217.

The cumulative distribution function (CDF) plot shows the proportion of patients discharged by a certain day for each group and is presented in Fig. 2.



Source: Elaborated by the authors.

**Figure 2.** Proportion of patients discharged by a certain day.

Based on this visualization and the analysis, the 1st day where the difference in the CDF between patients with positive and negative swab statuses starts to become more significant is on day 8.

To examine the relationship between HAI frequencies and 90-day mortality rates in patients with negative and positive control swabs, a comparative analysis was conducted. Among patients with negative control swabs, IRAS occurred in 16.67% of cases, whereas in those with positive control swabs, the incidence rose to 57.14%. This difference was found to be statistically significant with a  $p$ -value of 0.0118. Similarly, while 90-day mortality was absent in patients with negative control swabs, it was observed in 29.17% of cases among those with positive control swabs, with a  $p$ -value of 0.0077.

## DISCUSSION

LT contributes to the full spectrum of major risk factors for colonization and infection by MDRO, presenting a potentially dire situation, as both prior colonization<sup>19</sup> or infection,<sup>20</sup> as well as post-transplant infection,<sup>2</sup> are associated with increased mortality.

Bacterial infections are the leading cause (up to 60%) of death in the first 90 days after LT.<sup>21-22</sup> The emergence of MDRO poses a significant threat to global health, with specific challenges prevalent in low- and middle-income countries.<sup>23</sup>

The study evaluated the impact of a cleaning technological resource on a cohort of a very specific population that cannot avoid several risk factors for MDRO colonization. Critical thinking suggests that colonization is related to case severity. To assess this issue within the scope of analyzing the effectiveness of the technology under study, known risk factors were analyzed, such as the level of medical care, antibiotic exposure, muscle waist, obesity, diabetes, renal dysfunction, and acute-on-chronic liver failure. While risk stratification for LT is extensively discussed<sup>24</sup> and is beyond the scope of this text, validated indices such as BAR, SOFT, MELD 3.0, and ID2EAL were used. It is noteworthy that almost all variables showed no statistically significant differences between the groups, suggesting comparable baseline characteristics among the study cohorts.

Only one risk factor was significantly different, the cold ischemia time. Nevertheless, the longest observed cold ischemia time is still shorter than the usual 12-hour cut-off,<sup>25</sup> and, together with the absence of differences regarding post-operative graft function, it was not considered relevant.

It was observed that a negative control swab was more than twice as likely (OR 2.33) as positive ones in the aHPV group. This significant association between the cleaning method and the likelihood of achieving a negative control swab result aligns with the findings of a study of similar design. Passaretti et al.<sup>12</sup> found a 64% reduction in the risk of patient acquisition of MDROs in a busy, high-risk unit.

MDRO can survive on surfaces for extended periods ranging from days to months and may be transmitted from contaminated surfaces to the hands of healthcare workers, serving as a potential route of transmission to other patients.<sup>26-28</sup> Hand hygiene compliance was similar between groups, with only a slight, non-significant improvement after HPV implementation. Maintaining high compliance is challenging, but it remains the most effective and cost-efficient strategy to prevent cross-transmission of pathogens.<sup>16,29</sup>

Persistent contamination with MDRO despite the use of traditional cleaning and disinfection methods,<sup>30,31</sup> underscores the heightened risk associated with occupying rooms previously inhabited by colonized or infected patients,<sup>10</sup> thereby increasing the potential transmission of VRE,<sup>32</sup> MRSA,<sup>33</sup> *Acinetobacter baumannii*,<sup>34</sup> and CRE.<sup>35</sup> The coronavirus disease 2019 (COVID-19) pandemic has heightened an increase in outbreaks of multidrug-resistant infections.<sup>36</sup>

HPV is a sporicidal vapor-phase automated method capable of eliminating environmental reservoirs.<sup>9,37</sup> The known advantages of this system target recognized factors of hygiene failure and encompass reliable biocidal activity against a broad spectrum of healthcare-associated pathogens.<sup>38,39</sup> It facilitates the decontamination of room surfaces and equipment, proving useful for disinfecting complex equipment and furniture. Additionally, it does not necessitate the movement of equipment and furniture, a known limitation of ultraviolet irradiation. It leaves no residual residue, ensures uniform distribution in the room, and operates independently of the operator.<sup>40</sup>

Although not significantly different, it is important to note that the change in KPC isolation was more pronounced in the data (Fig. 1). The colonization or infection pathogen that was reduced in previous HPV studies is heterogeneous,<sup>41</sup> probably reflecting the specific flora of each hospital. Regarding the site of infection, SSI reduction was more pronounced, and as is known, it is the primary source of infection in liver transplants.<sup>2,20,22</sup>

The findings favor the use of HPV to reduce the likelihood of MDRO colonization, but the regular use of HPV presents several practical challenges. Disinfection is time-consuming, requiring sealing air vents and doors and vacating areas for the duration of the decontamination process.<sup>10,12</sup> Given the significant resources in time and money, previous questions from other colleagues are repeated: does it matter?<sup>11,27</sup>

The data revealed that, on average, patients with a positive swab result stayed 10 days longer than those with negative results. The findings suggest that the impact of swab status on the length of hospital stay becomes notably distinct around the end of the 1st week of hospitalization (8th day), when the difference in the proportion of patients discharged between the two groups begins to be more pronounced. This agrees with Chen et al.'s data,<sup>31</sup> which, in a large prospective multicenter trial, demonstrated that pathogen transmission occurs early, readily, and frequently. This could be a critical point for healthcare providers to consider when planning care and interventions for patients with different swab statuses.

Data analysis revealed a significantly lower frequency of HAIs in patients with negative control swabs compared to those with positive swabs. Similarly, analysis of 90-day mortality rates showed a significant difference between the negative and positive control swab groups. The established link between MDRO rectal colonization and infection in this specific scenario is well-documented in the literature.<sup>42,43</sup> However, due to the diverse range of pathogens encompassed by MDROs and their varying pathogenicity patterns,<sup>44</sup> ongoing discussion and analysis persist in this area. The association of rectal colonization with mortality has been previously demonstrated in the literature for various MDRO pathogens, including CRE, MRSA, VRE, and *A. baumannii*.<sup>19,45,46</sup>

It is worth recalling that LT exhibits unique characteristics favoring the colonization-infection pathway: dysbiotic gut microbiota colonized by MDROs, accompanied by alterations in the normal integrity of the mucosal epithelium or mucosal immunity.<sup>47</sup> These alterations may arise due to the liver disease itself<sup>48</sup> or be exacerbated by portal vein occlusion<sup>49</sup> during LT, in association with dysfunction of Kupffer and sinusoidal endothelial cells following liver reperfusion.<sup>50</sup>

MDROs pose a complex challenge in LT. Whole-genome sequence studies have illustrated that colonization is a highly dynamic and intricate process.<sup>51</sup> Once colonization occurs, effective eradication methods for these organisms are lacking,<sup>52</sup> and there is no standardized approach for antibiotic prophylaxis.<sup>53</sup> Furthermore, if infection arises, the limited drug armamentarium available is hindered by elevated costs in a public health system.

Improved cleaning and disinfection practices were sought, and HPV seems to provide them. Other technological resources are available,<sup>27</sup> and even “blitzkrieg” traditional cleaning policies have been proven to be effective.<sup>54</sup> Given the occurrence of recontamination following HPV room decontamination,<sup>55</sup> another challenge lies in determining the frequency of comprehensive ICU decontamination. It is important to underscore that automated disinfection will never reduce the total time needed for terminal cleaning and disinfection, as manual cleaning must always precede it.

The study design imposes limitations that must be noted. As this is a single-institution study focused on a very specific clinical population, the results may not be generalizable to other institutions with different MDRO profiles, infection control practices, acquisition rates, or patient risk factors. Institutional factors – such as staff compliance with hygiene protocols, availability of infection control resources, and the physical environment – can influence both the effectiveness of decontamination strategies and the observed outcomes. The frequency of pretransplant colonized patients (12%) was consistent with other studies.<sup>56</sup> Important potential confounders were not measured, such as compliance with surface cleaning, which may lead to residual contamination, introduce bias by misattributing results to HPV, and create variability across teams, compromising data reliability. Additionally, the lack of detailed data on antibiotic usage variability limits the analysis of selective pressure dynamics in the ICU.

The dynamics of MDROs may be better captured using big-data, at the population level,<sup>56</sup> but even those mathematical models will be based on individual-level data. Another inherent limitation of the study is that it is impossible to guarantee independence between individuals,<sup>57</sup> as those pathogens have an inherent communicable nature, and share healthcare professionals and physical installations. A favorable aspect of the present cohort study is that the intervention (cleaning) accumulates favorable empirical evidence, which would limit randomization in a clinical trial design due to ethical considerations.

The conclusion is that HPV system technology demonstrated efficacy in reducing rectal colonization by MDROs in a very specific LT cohort. Rectal colonization by MDROs resulted in more cases of HAI and reduced 90-day patient survival.

## CONFLICT OF INTEREST

Nothing to declare.

## AUTHOR’S CONTRIBUTION

**Conception and design:** Silveira F, Silveira FP, Itinose K; **Data analysis and interpretation:** Silveira F, Silveira FP, Silveira CRS; **Article writing:** Silveira F, Silveira CRS; **Critical revision:** Silveira F, Silveira FP, Facchi TLS, Costa ED, Itinose K; **Final approval:** Silveira F, Silveira FP, Silveira CRS, Facchi TLS, Costa ED, Itinose K.

## DATA AVAILABILITY STATEMENT

Data is available upon request.

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