Evaluation of nursing records on extracorporeal membrane oxygenation in trained multidisciplinary teams

ABSTRACT
Objectives: to compare the content of the nursing records regarding extracorporeal membrane oxygenation (ECMO) between the pre- and post-training periods of the multidisciplinary team. Method: retrospective study conducted in an adult intensive care unit with patients using ECMO, between 2012 and 2019. The information from the nursing annotations, evolutions and prescriptions on the ECMO was analyzed. Results: it included 194 nursing records, which showed an improvement in the quality of nursing evolution regarding information on ECMO in the post-training period. Among the information, the quality of the record on the circuit and membrane stands out. Conclusion: multidisciplinary training on ECMO was crucial for improving information in nursing evolutions. However, the continuity of training is essential for the appropriate maintenance of the nursing records that involve this support. Descriptors: Extracorporeal Membrane Oxygenation; Nursing Records; Nursing; Intensive Care Units.

RESUMO
Objetivos: comparar o conteúdo dos registros de enfermagem referente à oxigenação por membrana extracorpórea (ECMO) entre os períodos de pré e pós-treinamento da equipe multidisciplinar. Método: estudo retrospectivo realizado em uma unidade de terapia intensiva adulto com pacientes em uso de ECMO entre 2012 e 2019. Foram analisadas as informações das anotações, evoluções e prescrições de enfermagem sobre a ECMO. Resultados: foram incluídos 194 registros de enfermagem, que evidenciaram melhora na qualidade da evolução de enfermagem referente às informações da ECMO no período pós-treinamento. Dentre as informações, destaca-se a qualidade do registro sobre o circuito e a membrana. Conclusão: o treinamento multidisciplinar em ECMO foi fundamental para a melhoria das informações nas evoluções de enfermagem. Contudo, a continuidade de treinamentos se faz essencial para manutenção adequada dos registros de enfermagem que envolvem este suporte. Descritores: Oxigenação por Membrana Extracorpórea; Registros de Enfermagem; Enfermagem; Unidades de Terapia Intensiva.

RESUMEN
Objetivos: comparar el contenido de los registros de enfermería respecto a la oxigenación por membrana extracorpórea (ECMO) entre los períodos pre y post-entrenamiento del equipo multidisciplinar. Método: estudio retrospectivo realizado en una unidad de cuidados intensivos para adultos con pacientes bajo tratamiento de ECMO entre 2012 y 2019. Se analizó información de anotaciones, evoluciones y prescripciones de enfermería sobre ECMO. Resultados: se incluyeron 194 registros de enfermería, que señalaron una mejora de la calidad en la evolución de enfermería respecto a la información de ECMO en el período post-entrenamiento. Entre la información, se destaca la calidad del registro sobre el circuito y la membrana. Conclusión: el entrenamiento multidisciplinario en ECMO fue fundamental para mejorar la información en las evoluciones de enfermería. Sin embargo, la continuidad del entrenamiento es clave para el correcto mantenimiento de los registros de enfermería que involucran este apoyo. Descriptores: Oxigenación por Membrana Extracorpórea; Registros de Enfermería; Enfermería; Unidades de Cuidados Intensivos.

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INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is a highly complex support indicated for situations of respiratory or cardiorespiratory failure\(^1\). Over the last decade, there has been an increase in the use of this support, which implies the need for training of multidisciplinary teams, given the specificity of conducting care related to the ECMO system\(^2-3\). In this context, nursing records (NR) stand out because the management of ECMO involves the use of various materials and actions of the multidisciplinary team. Therefore, it is essential that the information is documented properly, with the aim of ensuring evidence on the procedures and care performed.

According to the registry belonging to the Extracorporeal Life Support Organization (ELSO), the use of ECMO has increased five-fold since the end of the first decade of the XXI century\(^3\). In addition, there has been an increase in the number of institutions considered excellence centers by ELSO in the last decade\(^3\). For a hospital institution to be considered an excellence center by ELSO, it requires the training of a multidisciplinary team in terms of ECMO care, in addition to the standardization of routines and protocols in relation to this support\(^4\).

ECMO is considered a highly complex support and requires several specific care for its management. Accordingly, specific training is necessary to provide safe and quality care\(^4,6\). ELSO recommends training the multidisciplinary team consisting of physicians, nurses and physiotherapists, who should be equally trained for decision-making in terms of support, although only the medical team is responsible for inserting and removing cannulas\(^4\). Concerning the nursing team, the nurse is responsible for the direct care of the patient, given the severity and complexity usually associated with the indication of support and, when trained, performs the management of the ECMO system\(^7\).

In a study that evaluated the impact of multidisciplinary training on ECMO, it was found that, after training the team, there was an increase in decannulations from 42% to 65% and a decrease in hospital mortality from 75% to 52%\(^3\). It was also noticed that, after the team training, the time between ICU admission and support start was reduced by almost half, due to the recognition of the indication of support earlier, which indirectly affects the clinical outcome\(^8\), in addition to impacting on the reduction of complications observed in the cannulas and in the patient and, consequently, on hospital costs\(^9\).

However, among the various factors that corroborate the quality of care provided, especially regarding the nursing team, NR stand out\(^10\). It is known that NR are constituted by the annotation, evolution and prescription performed by the nursing team and are crucial for the effectiveness of the nursing process or nursing care systematization (NCS)\(^11\). Through NR, it is possible to monitor the evolution of the health statuses of patients, evaluate the results of the interventions performed, improve communication between team members and have evidence for the billing systems of health operators, in addition to the fact that NR assume the nature of legal documentation in the face of legal bodies\(^12-13\).

Accordingly, considering the severity of the patient undergoing ECMO, associated with the high complexity and cost of the support, it is essential that NR contain essential information regarding the specific care performed\(^6,14\). From then on to the very present, there are no studies on the impact of multidisciplinary training on ECMO related to the quality of NR or regarding the specific information of this support.

Therefore, considering the importance of the quality of NR and the increase in the use of ECMO in recent years, the objective of the present study was to compare the content of the nursing annotations, evolutions and prescriptions regarding the quality of information on ECMO between the pre- and post-training periods of the multidisciplinary team for support.
EVALUATION OF NURSING RECORDS ON EXTRACORPOREAL MEMBRANE OXYGENATION

METHODOLOGY

This is a retrospective, before-and-after and observational study of a documentary nature conducted in an Adult Intensive Care Unit (AICU) of a large private hospital located in the city of São Paulo, SP. This AICU has a general characteristic and has 37 beds, divided into eight units designed to provide comprehensive care to patients requiring intensive care. It is noteworthy that the institution in question is considered an excellence center in terms of ECMO care by ELSO(3).

The sample obtained was of the convenience type and consisted of all the medical records of patients over 18 years of age admitted to the aforementioned AICU, who underwent ECMO between 2012 (start of the use of the support in the institution) and 2019. The wide time range is justified by the high complexity of this support, indicated for critically ill patients, which implies a restriction in its use and, consequently, in the total number of individuals in the sample. Illegible or incomplete medical records were excluded from the data collection. In all, 72 patient records were included.

Data collection was carried out by the researchers themselves, after approval by the ethics committee of the institution, from January to March 2020. The instrument for data collection was designed by the authors, containing information on NR related to specific care in terms of ECMO, which were filled in on the platform named Research Electronic Data Capture platform (REDCap)(15).

In the present study, NR consisted of nursing annotations, evolutions and prescriptions, and only the specific information regarding ECMO during the first three days of its use was analyzed. The content of the extracorporeal support to be analyzed was selected according to the recommendations issued by ELSO concerning the main points of care held by nursing(7).

Regarding nursing annotations, there were verifications of items such as: location and aspects of cannula insertion; ECMO flow and rotation; pre- and post-membrane pressure values; heater temperature; blender and sweep gas values; use of anticoagulant medications; and presence of complications.

As for nursing evolutions, the items checked were: location and aspect of cannula insertion; coloration of return and access routes; ECMO flow and rotation; pre- and post-membrane pressure values; heater temperature; blender and sweep gas values; information on anticoagulation (information on ml/h, or suspension together with the reason, and values of laboratory tests, such as ACT or APTT); presence or absence of whipping movements in the circuit; description of the circuit and membrane conditions (presence of fibrin, clot or air); pre- and post-gas values of the membrane and patient; and the existence of complications.

Finally, concerning nursing prescriptions, the following items on care were evaluated: dressing of cannula insertion; material for fixing the cannulas and circuit connections; signs of bleeding; changing the pre- and post-membrane pressure transducers and the level of distilled water contained in the heater; the circuit condition; the gas, blender and sweep gas connections; records of ECMO parameters (flow, rotation, pre- and post-membrane pressure values, sweep gas, blender and temperature); verification and adjustment of ECMO alarms as necessary; and verification of the equipment for the correct mains voltage.

Therefore, in order to consider whether NR were complete, they should contain the information described above, depending on the type of record analyzed. In addition, with the purpose of comparing the quality of NR, they were divided between the pre- and post-multidisciplinary training periods on ECMO.

In 2016, a group of professionals working in AICU was selected, consisting of physicians, nurses and physiotherapists, who aimed to systematize the care of patients undergoing ECMO to ensure a more specific, safe and quality care. The training of these professionals took place in a course provided by a Brazilian reference
in terms of ECMO, together with ELSO, with a workload of 60 hours.

This was the first training of professionals in this type of support in terms of AICU, since, before 2016, there were no specialists in this procedure in the AICU setting, where the care conducted were not standardized and the direct care of the ECMO equipment was performed by the perfusionist professional. Similarly, the documentation carried out by the nursing team was based on the routine established in the unit, without the description of specific or standardized information regarding the support.

After the training in 2016, the institutional protocol on ECMO was implemented, through the systematization of routines, and the standardization of information records related to the management of support, especially for nursing care. It is noteworthy that, after the training, the sizing of the professional staff of the nursing team for patients undergoing ECMO started to be performed by a nurse for the care of the ECMO equipment and for the general care of the patient.

In order to carry out the analyses, the data entered in the REDCap platform were imported by spreadsheets of the Excel-2007 program, from Microsoft Windows, and then they were conducted using the program named Statistical Package for the Social Sciences (SPSS), version 26. With the purpose of making comparisons among nursing records (annotation, evolution and prescription), patients were separated into two groups: pre-training and post-training.

Descriptive analysis was performed for all variables in this study, where qualitative variables were presented using absolute and relative frequencies. The inferential analysis of the variables of interest, with respect to qualitative data, was determined by the Chi-square and Fisher exact tests. The significance level adopted for the analyses was 5%.

The study followed the recommendations of Resolution nº 466/2012 of the Brazilian National Health Council and was developed after approval by the Research Ethics Committee of Israeli Hospital Albert Einstein under opinion nº 4.520.045 (CAAE 38607120.8.0000.0071).

### RESULTS

The medical records of 72 patients were included, of which none were excluded, which had 194 records related to nursing evolutions, nursing prescriptions and nursing annotations. Figure 1 shows the comparison between the nursing records considered complete between the pre- and post-multidisciplinary training periods. Regarding nursing annotations, the records considered complete went from 9.8% to 11.7%, with p=0.476, while they went from 13% to 87% in nursing evolutions, with p<0.001, and from 5.3% to 8.9% in nursing prescriptions, with p=0.159.

**Figure 1 – Comparison between the nursing records considered complete between the pre- and post-multidisciplinary training periods. São Paulo, SP, Brazil, 2019.**

![Figure 1](image-url)

Source: designed by the authors based on research data.

Table 1 shows the analysis of nursing annotations related to information on ECMO between the pre- and post-training periods of the multidisciplinary team. It was found that there were no significant post-training improvements in the total sample, and the best result was on anticoagulation (4.3% to 13.5%, p=0.087). It was also found that the post-training multidisciplinary annotations related to blender (0 to 6%, p=0.339), sweep gas (0 to 4%, p=0.547) and heater temperature (0 to 1%, p=0.999) improved, but all without statistical significance.
Table 1 – Analysis of nursing annotations related to information on ECMO between the pre- and post-training periods of the multidisciplinary team. São Paulo, SP, Brazil, 2019.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=194)</th>
<th>Pre-training (n=46)</th>
<th>Post-training (n=148)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannula location n(%)</td>
<td>56(28.9)</td>
<td>12(26.1)</td>
<td>44(29.7)</td>
<td>0.634*</td>
</tr>
<tr>
<td>Aspect of cannula insertions n(%)</td>
<td>54(27.8)</td>
<td>10(21.7)</td>
<td>44(29.7)</td>
<td>0.291*</td>
</tr>
<tr>
<td>ECMO flow n(%)</td>
<td>5(2.6)</td>
<td>1(2.2)</td>
<td>4(2.7)</td>
<td>&gt;0.999**</td>
</tr>
<tr>
<td>ECMO rotation n(%)</td>
<td>4(2.1)</td>
<td>1(2.2)</td>
<td>3(2.0)</td>
<td>&gt;0.999**</td>
</tr>
<tr>
<td>Blender n(%)</td>
<td>6(3.1)</td>
<td>-</td>
<td>6(4.1)</td>
<td>0.339**</td>
</tr>
<tr>
<td>Sweep gas n(%)</td>
<td>4(2.1)</td>
<td>-</td>
<td>4(2.7)</td>
<td>0.574**</td>
</tr>
<tr>
<td>Heater temperature n(%)</td>
<td>1(0.5)</td>
<td>-</td>
<td>1(0.7)</td>
<td>&gt;0.999**</td>
</tr>
<tr>
<td>Pre- and post-membrane pressure values n(%)</td>
<td>3(1.5)</td>
<td>1(2.2)</td>
<td>2(1.4)</td>
<td>0.558**</td>
</tr>
<tr>
<td>Anticoagulation n(%)</td>
<td>22(11.3)</td>
<td>2(4.3)</td>
<td>20(13.5)</td>
<td>0.087*</td>
</tr>
<tr>
<td>Intercurrence description n(%)</td>
<td>64(33.3)</td>
<td>18(40.0)</td>
<td>46(31.3)</td>
<td>0.278*</td>
</tr>
</tbody>
</table>

ECMO: extracorporeal membrane oxygenation; *Chi-square test; **Fisher exact test.
Source: designed by the authors based on research data.

Table 2 shows the analysis of nursing evolutions related to information on ECMO between the pre- and post-training periods of the multidisciplinary team. It is noted that there was improvement in most of the records observed, with emphasis on the presence of whipping (from 8.7% to 60.8%, p <0.001), followed by blender (from 34.8% to 81.8%, p <0.001) and sweep gas (from 39.1% to 85.1%, p <0.001).

Table 2 – Analysis of nursing evolutions related to information on ECMO between the pre- and post-training periods of the multidisciplinary team. São Paulo, SP, Brazil, 2019.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n=194)</th>
<th>Pre-training (n=46)</th>
<th>Post-training (n=148)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannula location n(%)</td>
<td>152(78.4)</td>
<td>27(58.7)</td>
<td>125(84.5)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Aspect of cannula insertions n(%)</td>
<td>144(74.2)</td>
<td>26(56.5)</td>
<td>118(79.7)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Coloration of return and access routes n(%)</td>
<td>93(47.9)</td>
<td>6(13.0)</td>
<td>87(58.8)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Adjustment of ECMO alarms n(%)</td>
<td>25(12.9)</td>
<td>-</td>
<td>25(16.9)</td>
<td>0.003**</td>
</tr>
<tr>
<td>ECMO flow n(%)</td>
<td>154(79.4)</td>
<td>27(58.7)</td>
<td>127(85.8)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>ECMO rotation n(%)</td>
<td>141(72.7)</td>
<td>20(43.5)</td>
<td>121(81.8)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Pre- and post-membrane pressure values n(%)</td>
<td>95(49.0)</td>
<td>21(45.7)</td>
<td>74(50.0)</td>
<td>0.606*</td>
</tr>
<tr>
<td>Heater temperature n(%)</td>
<td>123(63.4)</td>
<td>15(32.6)</td>
<td>108(73.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Blender n(%)</td>
<td>137(70.6)</td>
<td>16(34.8)</td>
<td>121(81.8)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Sweep gas n(%)</td>
<td>144(74.2)</td>
<td>18(39.1)</td>
<td>126(85.1)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Anticoagulation n(%)</td>
<td>151(77.8)</td>
<td>31(67.4)</td>
<td>120(81.1)</td>
<td>0.051*</td>
</tr>
<tr>
<td>Presence of whipping n(%)</td>
<td>94(48.5)</td>
<td>4(8.7)</td>
<td>90(60.8)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Circuit and membrane conditions n(%)</td>
<td>125(64.4)</td>
<td>13(28.3)</td>
<td>112(75.7)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

(continues)
Table 3 shows the analysis of nursing prescriptions related to information on ECMO between the pre- and post-training periods of the multidisciplinary team. It is possible to observe that there was a reduction in the post-training records, which were found in the observation of the presence of bleeding (from 80.4% to 45.9%, \( p \leq 0.001 \)), followed by dressing change (from 60.9% to 33.1%, \( p = 1000.1 \)). Although the schedule for changing pressure transducers (from 0 to 2.7%, \( p=5.74 \)) and checking the water level in the heater (from 0 to 2%, \( p=0.999 \)) improved after the training, they did not obtain statistical significance.

**DISCUSSION**

Written documentation is a way of ensuring the continuity of care provided, as well as maintaining the quality and safety of care. The results obtained show that there was an improvement in the quality of information related to ECMO in nursing evolutions after the multidisciplinary training period. However, it was not possible to observe an effective improvement of nursing annotations and prescriptions in the period after training. It is worth underlining that only the professional nurse of the nursing team participated in the training of the support in question, in view of his/her direct responsibility in the care of critically ill patients[7].
In the care of critically ill patients, it was found that more than 67% of nursing annotations had inadequacies or incomplete information related to the recording of signs and symptoms\(^{(16)}\). The incompleteness of nursing annotations may be influenced by overload of work, lack of continuing education, demotivation, insufficient remuneration and inadequate team communication\(^{(17)}\). In the context of ECMO-associated care, it is underlined that the nursing technician is not the professional of the nursing team indicated to provide direct care to the patient due to the clinical severity and complexity\(^{(7)}\). Accordingly, there is a lack of knowledge of the information to be documented regarding the support by the nursing technician and, even, the direct non-participation in the care provided at the bedside\(^{(17)}\).

On the other hand, the improvement of information on ECMO in nursing evolutions was relevant and the use of training with the objective of improving NR has been found in the literature\(^{(18)}\). In a North American study conducted in 2019, it was observed that, after the implementation of an instrument aimed at evaluating incontinence-associated dermatitis among nurses, there was a significant improvement in the quality of documentation, from 35.4% to 84.2%, with p<0.001\(^{(18)}\).

Therefore, it is clear that there is an improvement in the quality of NR in Home Care after the training of professionals in relation to the proper elaboration of records\(^{(19)}\). An increase of 80% in the compliance of the records after the training should be highlighted, in addition to the impact on the better adherence of patients to treatment\(^{(19)}\).

According to a Brazilian study conducted in 2019, which compared the effect of the educational program on the quality of the records related to the nursing process, through the application of the instrument named Quality of Nursing Diagnoses and Interventions and Outcomes (Q-DIO)\(^{(20)}\), an increase in the Q-DIO score was observed in the period after the implementation of the educational program, from 8.3 ± 4.6 to 18.3 ± 10.0, with p = 0.003\(^{(20)}\). Similarly, another Brazilian study, which evaluated the quality of NR before and after training and implementation of the Q-DIO instrument in cardiovascular units, showed an increase in the Q-DIO score from 14.8±5.7 to 29.0±10.5, with p=0.003\(^{(21)}\). In this sense, the impact of educational interventions on the quality of NR is clear.

Nevertheless, some items still have lower adherence even after training. Thus, among the main difficulties encountered, which were pointed out by nurses in the elaboration of nursing evolutions, one can mention the lack of time for a proper design\(^{(22)}\). Other factors, such as the performance of activities outside the care context, in addition to the time required for the necessary care and the insufficient number of professionals, contribute towards the unavailability of time for the writing of NR\(^{(22)}\). Among the implications of these factors pointed out by nurses, one can also mention the loss of accuracy of information on the care provided and, consequently, there is a repercussion on the quality and reliability of NR\(^{(22)}\).

Similarly, in a Brazilian study conducted in 2019, which sought to understand perception of nurses in relation to the relevance of NR to nursing care, it was noted that professionals focus on care, to the detriment of systematic records of their care actions\(^{(19)}\). Thus, it is clear that the records made must be monitored and, consequently, constant training on this theme must be carried out\(^{(23)}\).

Therefore, it is worth underlining that patients undergoing ECMO are in critical conditions, and the nursing workload is significant\(^{(24)}\). In an Italian study, which evaluated the nursing workload by the Nursing Activities Score (NAS) in patients submitted to ECMO, NAS was mostly close to or greater than 100 points\(^{(24)}\). In addition, the recommendation for the division of nurses by patients is 1:1, given the demand for necessary care\(^{(24)}\).

With respect to nursing prescriptions, in an analysis of the dressing prescriptions made
by nurses and physicians regarding the clarity and suitability of the product prescribed, it was noticed that 93.6% of the records were incomplete about the conduct to be performed\(^{(25)}\), which can lead to unspecific care provided to the patient, in such a way as to jeopardize the correct treatment that should be followed\(^{(25)}\).

On the other hand, NR are essential elements in the process of auditing the care provided and controlling hospital costs. In a Brazilian integrative review conducted in 2018, which analyzed the relationship between NR and hospital billing, it was shown that there is an association between NR and hospital costs, since NR enable the financial maintenance of the health service\(^{(26)}\).

In addition, the cost of using ECMO for five days of therapy is around R$34,000.00\(^{(27)}\). Of this amount, approximately R$26,000.00 is related to circuit, cannulas and medical-hospital materials and R$6,000.00 to daily rates\(^{(27)}\). Therefore, it is obviously a high-cost therapy, thus requiring appropriate physical, material and human structure, which, through a quality NR, can contribute towards the organization of all expenses and avoid possible gluts of health operators. Above all, it is worth emphasizing now the legal nature of NR, since one can have legal evidence of the actions provided to patients through written communication regarding the care provided\(^{(13)}\).

In summary, the NR of patients submitted to ECMO is crucial for the quality and safety of care. The clear favorable impact of training on the multidisciplinary team regarding the improvement of nursing evolutions reinforces the need for specific training on NR. Of course, the systematization of care for the appropriateness of actions and conduct has proven to be crucial for the effectiveness of NCS.

Furthermore, the present study has limitations because it analyses only one center, which makes it difficult to obtain data for more robust and comprehensive analyses. Accordingly, it is necessary to carry out prospective studies that verify the improvement in nursing annotations and prescriptions after new training regarding ECMO directed to nursing teams.

### CONCLUSION

In this study, it was found a small improvement in nursing annotations and prescriptions regarding the specific content of ECMO after multidisciplinary training on this therapy. Nevertheless, the significant improvement of information in nursing evolutions after multidisciplinary training should be highlighted. Accordingly, it is necessary to improve nursing annotations and prescriptions related to information on ECMO through new training, which should be developed and applied to the nursing team so that the effects on the quality of these records are evaluated again in the future.

It must be considered that the improvement in the quality of information in nursing evolutions should, in theory, reflect an increase in nursing prescriptions, which did not happen. Therefore, it is plausible to state that the efforts for the progress of nursing records must be tireless, since the nursing care arising from the prescription has the ability to positively influence the nursing care provided to the seriously ill patient.

With respect to nursing annotations, elaborated mostly by mid-level professionals, training aimed at the quality of information should consider the needs in relation to training, professional experience, mechanization of work and impact of the record on the continuity of the care process with the patient using high and complex technology, such as ECMO. Therefore, at this point, the nurse, as leader of the nursing team, must promote permanent education to his/her collaborators, with a view to elaborating nursing annotations that reflect the care provided and the respective responses of the patients.

### REFERÊNCIAS


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