CENTRIFUGAL VERSUS MEMBRANE THERAPEUTIC PLASMA EXCHANGE (TPE): A CHILEAN, MULTI-CENTER, COST-COMPARISON STUDY

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INTRODUCTION

Therapeutic Plasma Exchange (TPE)

- Therapeutic plasma exchange (TPE) or plasmapheresis is an extracorporeal medical therapy. The blood of the patient goes through a medical device that separates plasma — which contains several molecules such as antibodies, complement and cytokines — from the other cellular components.[1][2] This plasma is then eliminated and replaced by a colloid solution, or a combination of colloids and crystalloids.[3] TPE is commonly used in several clinical departments including, among others, neurology, hematology, nephrology, cardiology, rheumatology, hepatology, and immunology.[2][4][5]
- TPE is performed through two different technologies depending on the medical device:
  - In centrifugal TPE (cTPE), the device completes plasmapheresis using centrifugal force which separates particles based on their size, form, viscosity and density.
  - In membrane TPE (mTPE), the device completes plasmapheresis using a filtration process which runs the fluid through highly permeable membranes with determined thicknesses and specific pore sizes.[6]
- These two TPE technologies, due to their distinct plasmapheresis performance, present different technical, economic, clinical, operational and social elements.[2][6] Yet only a few studies exist that compare both types.[7][8]

COST DRIVERS AND ASSUMPTIONS

The cost of the medical device, its maintenance and depreciation

- In Chile, many healthcare centers maintain a rental contract for medical devices with a medical tech company. In these cases, the center does not buy the device or pay for its maintenance or depreciation, but the center must purchase a minimum annual number of disposable sets or filters (usually 200).
- In this model it is assumed that all medical devices are sold by the medical tech company to the healthcare center, and that the cost for centrifugal devices ranges from USD $50,000 to USD $60,000; while the cost of membrane devices ranges from USD $20,000 to USD $25,000. The maintenance costs are lower for centrifugal than for membrane devices. Centrifugal devices cost between USD $600 and USD $1,000 to maintain; membrane devices cost between USD $1,500 and USD $2,500 to maintain. Both types of devices will depreciate in a time span of between seven to twelve years.

Disposable sets or filters and additional material

- To perform TPE, a disposable set or filter to connect the patient with the medical device is required. Since there are several devices of both types (membrane and centrifugal) in the marketplace, a cost range which takes into consideration local Chilean data and literature is assumed to be between USD $300 to $350 and USD $215 to $275, respectively. Furthermore, as membrane devices might require additional materials such as connection tubes and exchange sets, these costs are included as well. [9][10] See **Table 1.**

Central or peripheral catheter access

- cTPE can be performed with a central access or peripheral access. The latter has two possible protocols: two access points/needles or a single access point/needle (also known as single-needle).
- mTPE can only be performed with a central access due to the high-flow levels required to filter properly.
- Peripheral access is considered the most cost-effective and to yield the best patient outcomes, as 1) the catheter is cheaper; 2) the set-up procedure is easier and faster; 3) it has fewer adverse events, such as bacteremia; and 4) it is better tolerated from the patient perspective.[11] The peripheral catheter is expected to be changed for each TPE procedure. On the other side, a central catheter is expected to be placed during the full TPE treatment and it might be changed only in case of technical or clinical force majeure.
- Even though cTPE should always be performed with peripheral access due to its clear advantages, for this study three models were used to capture the following cTPE utilization rates: 100% central access; 50% central access; 0% central access.[7][12][13][14]

Healthcare professionals' salaries and TPE procedure times

- To allocate healthcare professionals' salaries to the TPE procedure times, it is assumed that one nurse or technician will each perform only one TPE; and one physician will supervise two TPE procedures simultaneously.
- It is assumed the annual salary of nurses ranges between USD $18,000 to USD $28,000; and the annual salary of physicians ranges from USD $35,000 to USD $75,000. The annual range of working days is assumed to be from 200 to 250 days with eight working hours per day.[9][15]
- The TPE procedure times are obtained from the literature and are divided by 1) the time required to prepare the device and disposable sets and conduct a TPE procedure, 2) the time required to restart the TPE process due to a technical event, and 3) the time required to reinsert the needle in case of a technical or clinical event.[12]
- cTPE performs the first two instances more quickly than mTPE, allowing healthcare professionals to perform other tasks and decreasing bed retention time so beds can be used for other patients.[16][17]

Adverse events

- The most extensive worldwide report of approximately 45,000 TPE procedures confirms that mTPE is twice as likely to result in an adverse event compared with cTPE. In most of the mild and moderate adverse events, it is necessary to change the catheter and/or reinsert the needle. For the severe adverse events, it is necessary to immediately stop the TPE procedure.[18] Therefore the costs allocated to address the adverse events are based on the costs related to the time required to reinsert the needle, restart the TPE procedure and/or perform a completely new TPE procedure (required only for severe adverse events).
- It is important to highlight the consequences of adverse events on patients from a clinical and psychosocial perspective. However, this study does not assess the psychosocial impact related to the more adverse events of mTPE from a cost perspective.

Anticoagulation and clotting events

- A clotting event impedes the ability to perform a TPE procedure when blood that flows through the extracorporeal circuit clots. Consequently, an anticoagulant is used in most TPE procedures. Anticoagulant citrate dextrose solution A (ACD-A) is considered the best option to avoid clotting in the extracorporeal circuit. cTPE with Spectra Optia® Apheresis System should always be performed with ACD-A. For cTPE, the cost range for ACD-A is assumed to be between USD $10 and USD $15. For mTPE, heparin is used as well as ACD-A. Heparin is a cheaper anticoagulant than ACD-A. For mTPE, the cost range for the anticoagulant is assumed to be between USD $2 and USD $15.
- Clinical studies confirm the correlation between mTPE and clotting events, with clotting events occurring in up to 67% of the procedures performed. When an event occurs, the filter and/or disposable set should be changed and/or the TPE procedure should be terminated.[4][12][19]
- However, there are published reports from Colombian healthcare centers, such as Hospital Universitario San Ignacio, that describe 500 mTPE procedures without using any anticoagulant solution for the extracorporeal circuit and having only one clotting event (0.002%).[20][21] Although this percentage differs greatly from the frequency described in the other literature, this study uses a range of clotting events for mTPE between 0% to 67%.
- A clotting event during cTPE has never been reported in any publication. This also confirms that peripheral access, on top of its benefits, has never had any clotting event. However, as a potential clotting event could occur with cTPE, this study uses a range for clotting events for cTPE between 0% to 1%.

OBJECTIVES

- This study aims to illustrate all the determinants of TPE by using a protocol and statistical model that integrate Chilean regional information as well as information extracted from literature review. This study also aims to highlight the differences between centrifugal and membrane devices; clarify the assumptions used in their comparison; and establish the best device to realize TPE.

METHODOLOGY

- The World Health Organization (WHO) guidelines on assessing the cost-effectiveness between two or more medical technologies were followed to analyze the determinants of TPE. [22] Drawn from a review of the literature, the parameters of this study are the 1) ***direct costs***, which include the medical device with its maintenance and depreciation; disposable set/filter and additional material; and the central or peripheral catheter 2) ***indirect costs***, which include healthcare professionals' salaries and the use of hospital resources related to the TPE procedural time.
- The costs associated with adverse events, clotting events and TPE access (central and peripheral) are included as well. [2] [9] [12] To define these parameters, incidence values extracted from clinical publications are used and, for the different TPE procedural times, averages among the publications are used. A cost or range of costs is linked to each one of the values. When there are cost ranges, the lowest and highest values found in the literature or local data are used. All costs extracted from the literature are adjusted to the Chilean economy (2019). See **Table 1.**
- Three statistical models are used and populated with the above-mentioned parameters. For each one, a specific percentage of cTPE access has been applied: 100% central access; 50% central access; 0% central access. 1,000 iterative scenarios have been computerized for each one of them and subsequently analyzed.
- Results are based on the average of the three statistical models.

Parameters	Scenarios	
Type of TPE	centrifugal	membrane
Quantity of TPE performed annually	30 - 300	
Required quantity of TPE to fully treat one patient	4 | 5 | 6	
Medical device costs (USD $)	50,000 - 60,000	20,000 - 25,000
Medical device maintenance annually (USD $)	600 - 1,000	1,500 - 2,500
Medical device depreciation time (years)	7 - 12	
Disposable set/filter (USD $)	215 - 275	300 - 350
Additional material for the medical device and/or disposable set/filter (USD $)	0	5 - 15
Anticoagulant solution (USD $)	10 - 15	2 - 15
Peripheral access (catheter and placement costs) (USD $)	10 - 20	-
Central access (catheter and placement costs) (USD $)	100 - 500	
Annual salary for a nurse (USD $)	18,000 - 28,000	
Annual salary for a physician (USD $)	35,000 - 75,000	
Annual working days	200 - 250	
Time for device and disposable set preparation and TPE procedure (min)	101 - 144	170 - 181
Time for restarting TPE process due to a technical event (min)	10 - 22	40 - 46
Time for needle reinsertion in case of technical/clinical event (min)	10	
Mild/moderate adverse events (percentage per TPE) (%)	5.6	9.5
Severe adverse events (percentage per TPE) (%)	0.6	1
Clotting events (percentage per TPE) (%)	0 - 1	0 - 67
Clotting events that require the termination of the TPE procedure (%)	60	
Clotting events that require the replacement of the disposable set/filter (%)	40	

Table 1. Parameters and values included in the cost models.

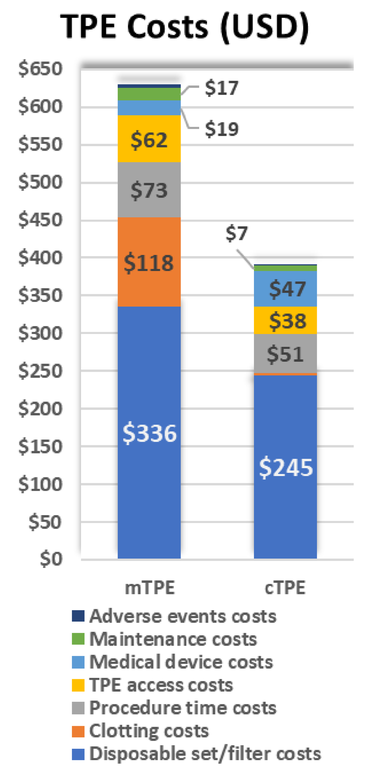

Figure 2. Costs of mTPE and the average between the three cTPE-percentage-access scenarios

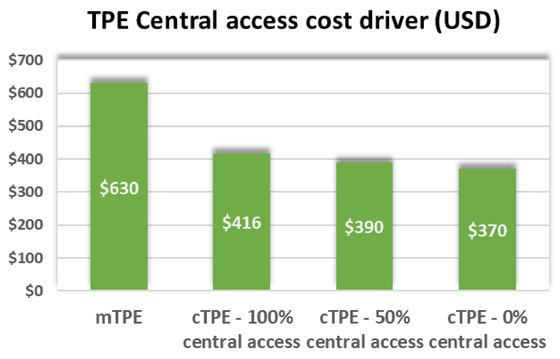

Figure 1. Global costs for mTPE; cTPE – 100% central access; cTPE – 50% central access; cTPE – 0% central access.

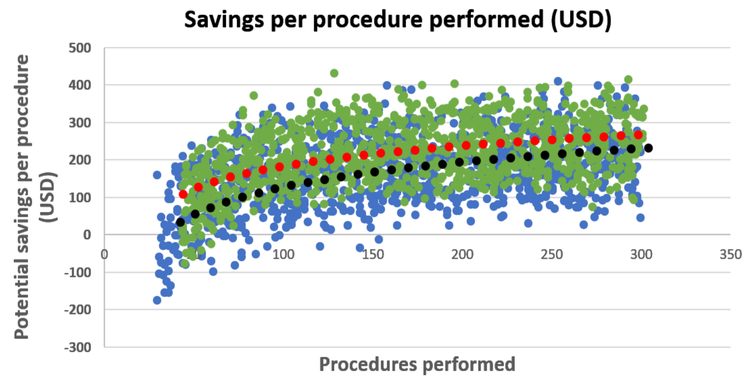

Figure 3. Computerized analysis of mTPE vs. cTPE in the least favorable scenario (100% central access, blue dots with black trendline) and cTPE in the most favorable scenario (0% central access, green dots with red trendline). Each green/black dot represents one of the 1,000 iterations of the model. Both trendlines follow a logarithmic curve.

RESULTS

- The average cost for mTPE is USD $630.The average cost for cTPE with 100% central access is USD $416. The average cost for cTPE with 50% central access is USD $390. And the average cost for cTPE with 0% central access is USD $370. See **Figure 1**.
- In 96% of the analyzed scenarios between mTPE and the three cTPE options, cTPE was more cost-effective. Classified by the impact on total costs, the most relevant cost drivers between the technologies are 1) disposable set/filter 2) clotting events 3) TPE procedure time 4) TPE access. See **Figure 2.** The only favorable parameter for mTPE over cTPE is the lower cost of the medical device.
- Considering the cost of the medical device is absorbed and distributed over the depreciation time and the procedures performed each year, the more TPE procedures that are performed, the cheaper cTPE becomes. **Figure 3** presents the positive correlations between potential savings and more TPE procedures performed, considering mTPE versus cTPE are performed with 100% central access (blue dots) and with 0% central access (green dots).
- If a healthcare center performs more than 30 cTPE annual procedures 100% with peripheral access, it is highly probable that the center will gain economic, operational and clinical benefits. However, if the hospital performs cTPE with only central access, the center will have to perform proportionally more cTPE annual procedures to gain those similar benefits. See **Figure 3**, trendline curves.
- There is a time difference of up to 41 minutes between the two systems, to prepare the device and disposable sets and complete a TPE procedure. The cTPE process occurs more quickly and efficiently than mTPE. See **Figure 2.** Consequently, considering an annual average of 165 TPE procedures, cTPE allows the nurse to allocate 6,600 minutes or 110 hours or around 14 working days annually for other healthcare tasks. The physician will be able to allocate half of them (seven working days).

CONCLUSION

- Analysis of the clinical and technical values extracted from the literature review along with cost data from Chilean healthcare centers confirms that cTPE is the most cost-effective and cost-efficient system in 96% of the analyzed scenarios, yielding better health outcomes, fewer adverse and clotting events, and the option to perform TPE with a peripheral access.
- Furthermore, the small percentage (4%) of mTPE scenarios that position mTPE as more cost-effective than cTPE exists only because of the lower cost of the medical device. If both devices were placed under the same annual minimum procedure requirements, the only favorable parameter for mTPE would be omitted. Thus, 100% of the scenarios would favor cTPE.
- Faster cTPE procedure times, compared with mTPE, allow professionals to allocate more time to other healthcare tasks, optimizing the efficiency of the healthcare center and the patient's attention and experience.

DISCUSSION

- The values extracted from the literature review might differ from the local data of Chilean healthcare centers, especially the ones related to adverse events, clotting events and TPE procedure times. Therefore, the authors of this study heartily recommend — and are available for any consultation and/or support — that each healthcare center which performs TPE execute a similar study using their local values. In this way, more exact and precise data can be obtained, with more internal and external validity, and thus better depict the current situation in Chile.

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