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Trends in corneal transplantation from 2001 to 2016 in Brazil

Tendências no transplante de córnea de 2001 a 2016 no Brasil

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ABSTRACT | A retrospective and analytical study was conducted by using data from the National Transplantation System on 184,575 corneal transplantations performed between January 2001 and December 2016 in order to analyze the trends in corneal transplantation from 2001 to 2016 in Brazil. The Cochran-Armitage test, analysis of variance, and Duncan's multiple comparisons were used to verify the existence of trends, compare the mean values between regions, and verify the mean differences, respectively. A significance level of 5% was used for all tests. The analysis showed that there was a 2.4-fold increase in the number of corneal transplantations (from 6,193 [35.2 per million people (pmp)] to 14,641 [71 pmp]; p<0.001), a 50.7% increase in the efficacy of meeting the population's demand for corneal transplantation (from 35.3% to 53.2%; p<0.001), an 11-fold increase in the number of corneal transplantation centers (from 32 to 356), and a 2.5-fold increase in the number of corneal transplantation teams (from 276 to 688) in Brazil during the period studied. The waiting list for corneal transplantation decreased by 45.4% (from 23,549 [123 pmp] to 12,865 [62.4 pmp]; p<0.001), and the corneal transplantation teams performed about 19 corneal transplantations per year. The best indices were observed in the southern, midwestern, and southeastern regions, and the worst indices were in the northern and northeastern regions. Brazil has been improving its capacity to perform corneal transplantation in the past 16 years, although this improvement varies across regions. However, the population's demand for corneal transplantation is yet to be satisfactorily met, primarily due to the low number of corneal donations.

Keywords: Health profile; Corneal diseases; Corneal transplantation; Directed tissue donation; Brazil

RESUMO | Estudo retrospectivo e analítico, baseado em dados do Sistema Nacional de Transplantes de 184.575 transplantes de córnea realizados no período de janeiro de 2001 a dezembro de 2016, com o objetivo de analisar as tendências do transplante de córnea no Brasil de 2001 a 2016. Os testes de Cochran-Armitage, análise de variância e comparações múltiplas de duncan foram realizados para verificar a existência de tendência, comparação de médias entre regiões e verificação da diferença média, respectivamente. Um nível de significância de 5% foi utilizado em todos os testes. No Brasil, houve um aumento: de 2,4 vezes no número de transplantes de córnea (de 6.193 [35,2 pmp] para 14.641 [71 pmp] - p<0,001); de 50,7% na eficácia de atender a demanda populacional de transplantes de córnea (de 35,3% para 53,2% - p<0,001); de 11 vezes no número de centros de transplantes de córnea (de 32 para 356); e de 2,5 vezes no número de equipes transplantadoras de córnea (de 276 para 688). A lista de espera para o transplantes de córnea diminuiu em 45,4% (de 23.549 [123 pmp] para 12.865 [62,4 pmp] - p<0,001). A produtividade das equipes de córnea ao longo dos anos foi de 19 transplantes de córnea ao ano. Os melhores índices foram apresentados nas regiões Sul, Centro-Oeste e Sudeste e os piores no Norte e Nordeste. O Brasil, embora de forma heterogênea entre as regiões, vem melhorando a capacidade de realizar o transplante de córnea nos últimos 16 anos, porém a demanda populacional por transplante de córnea ainda não é adequadamente atendida, principalmente devido ao baixo número de doações de córnea.

Descritores: Perfil de saúde, Doenças da córnea; Transplante de córnea; Doação dirigida de tecido; Brasil

INTRODUCTION

Corneal diseases account for about 4%-5% of reversible blindness worldwide[1-2]. If not properly treated, these diseases can significantly impact the social and psychological aspects of the affected persons, such as social isolation, cognitive impairment, accidents, depression, family dependence, and suicide[1,3-6].

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Corneal transplantation (CT), an effective treatment for several serious corneal diseases, primarily aims at restoring corneal transparency[7-9]. Good postoperative visual results are attributed to the use of advanced surgical paraphernalia such as wires with thinner diameters, thinner needles, precise surgical materials, surgical microscopy with good image definition, knowledge of endothelial function, and femtosecond laser[10-12].

The United States is a world reference for performing CT: In 2016, 62 eye banks were registered, 136,318 corneas were donated, and 82,994 CTs were performed in the country. The Eye Bank Association of America, founded in 1961, is a not-for-profit organization of eye banks dedicated to the restoration of sight through the promotion and advancement of eye banking[13]. In the United States, patients pay for the processing and transplantation costs either out of pocket or through health insurance plans, with the exception of very poor patients who benefit from government programs[14].

Founded in 1997, the Sistema Nacional de Transplantes (SNT) is part of the Brazil's Ministry of Health responsible for the control and monitoring of all stages of CT[15]. The Sistema Único de Saúde (SUS), Brazil's publicly funded healthcare system, finances more than 95% of transplantations and provides a partial subsidy on immunosuppressive drugs for all patients. The SUS covers the entire cost of the family interview, recovering a healthy cornea, and processing the recovered cornea by the eye bank; under no circumstances does the patient pay for a donated cornea. Patients who choose to undergo surgery outside the accredited SUS network can use their health insurance or pay out of pocket. Over the years, the official amount paid by the Brazilian government has remained the same despite high inflation rates[14].

In the Brazilian literature, few studies have investigated the process of donation, collection, storage, and distribution of tissues in Brazil for the purpose of identifying errors, minimizing difficulties, and improving national results[14,16-22].

This review aims to analyze the trends in CT from 2001 to 2016 in Brazil.

METHODS

This study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board/Ethics Committee of the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (protocol number 099/14, session 04/16/2014).

A descriptive, retrospective database review was performed by the author between October and December 2017. The data for 184,575 corneal transplants performed between January 2001 and December 2016 were retrieved from the computer database of SNT[15].

The following variables were analyzed in Brazil and Brazilian regions for each year: (1) number of CTs; (2) number of CTs per million people (pmp); (3) number of CT centers; (4) number of CT teams; (5) number of individuals on the waiting list for CT in December; and (6) number of individuals on the waiting list for CT pmp.

The Brazilian regions studied were categorized as follows: North, Northeast, Midwest, Southeast, and South. These regions are shown in the geographical map of Brazil in appendix 1.

From 2001 to 2009, SNT used the Brazilian population determined from the 2000 Brazilian Institute of Geography and Statistics (IBGE)[23] census to calculate pmp rates in Brazil and in the Brazilian regions. The population from 2010 to 2014 was based on the 2010 IBGE census. From 2015 onward, SNT used the modified annual population rate estimated by IBGE. As the population number interferes directly with the values used and the analysis performed, the TC pmp rate and the number of patients in the waiting list pmp were recalculated in October 2017 for the present study by taking into consideration the population estimated by the IBGE since 2001, which is closer to reality.

The indicator of the efficacy of meeting the population demand for CT (DCT) expressed as a percentage was

Appendix 1. Geographical map of Brazil.

calculated based on the following ratio: DCT = CT / CT + WL, where CT is the number of CTs performed per year and WL is the number of individuals on the waiting list for CT in December of each year.

The number of patients on the waiting list for CT from 2001 to 2007, necessary to calculate the DCT for those years, was not disclosed by SNT. Therefore, the DCT for those years was not calculated in this study.

The productivity indicator of CT teams (P) was calculated based on the following ratio: P = CT/MT, where CT is the number of CTs performed per year and MT is the number of CT teams per year. Decimal places were not included in the productivity indicator of the CT teams; thus, decimal values greater ≥5 were rounded up and values <5 were not considered. Data that were not provided by SNT are indicated in the tables 1 and 3.

Quantitative variables were expressed as absolute values. Trend verification for the series of CT pmp number, waiting list pmp, and DCT was performed by using the Cochran-Armitage test. Comparison of the mean CT pmp number, waiting list pmp, productivity of CT teams, and DCT by region during the period studied was performed by using Analysis of Variance (ANOVA). When a difference of means was identified, Duncan's multiple comparisons were used to identify Brazilian regions with different means, maintaining the level of global significance.

A significance level of 5% was used for all statistical tests. The Cochran-Armitage test was performed using the statistical software SAS 9.3 and other analyses were performed using SPSS v20.0. For the construction of charts and tables, Microsoft Excel® 2010 software was used.

RESULTS

Table 1 shows the number of annual CTs, number of CT pmp, number of individuals on the waiting list for CT, number of individuals on the waiting list for CT pmp, efficacy of meeting the demand for CT (DCT), number of CT centers, number of CT teams, and productivity of CT teams from 2001 to 2016 in Brazil. SNT did not provide data regarding the number of individuals on the waiting list for CT from 2001 to 2007; therefore, it was impossible to calculate the DCT/Y for these years.

There was a 2.4-fold increase in the number of CTs (from 6,193 [35.2 pmp] to 14,641 [71 pmp]; p<0.001)

Table 1. Number of corneal transplantations, number of corneal transplantations per million people, waiting list for the procedure, waiting list for the procedure per million people, efficacy of meeting the demand for corneal transplantation, number of corneal transplantation centers, number of corneal transplantation teams, and productivity of corneal transplantation teams from 2001 to 2016 in Brazil

Year	Transp	Trans/pmp	Waiting	Waiting/pmp	DCT (%)	Centers	Teams	Prod
2001	6,193	35.2	NA	NA	NA	32	276	22
2002	6,556	36.8	NA	NA	NA	172	526	12
2003	7,556	41.8	NA	NA	NA	182	587	13
2004	8,394	45.9	NA	NA	NA	200	645	13
2005	9,970	53.8	NA	NA	NA	207	609	16
2006	10,382	55.4	NA	NA	NA	222	622	17
2007	11,419	60.3	NA	NA	NA	233	586	19
2008	12,825	67.0	23,549	123.0	35.3	242	618	21
2009	12,723	65.7	23,756	122.7	34.8	254	626	20
2010	12,923	66.1	21,883	111.9	37.1	268	663	19
2011	14,838	75.2	17,559	89.0	45.8	280	649	23
2012	15,141	76.0	10,249	51.4	59.6	292	670	23
2013	13,765	68.5	8,608	42.8	62.3	306	664	21
2014	13,456	66.4	10,734	52.9	55.6	331	681	20
2015	13,793	67.5	12,686	62.0	52.0	355	671	21
2016	14,641	71.0	12,865	62.4	53.2	356	688	21
p	-	<0.001	-	<0.001	<0.001	-	-	-

p value= Descriptive level of the Cochran-Armitage test for trend.
Transp= number of corneal transplantations; Trans/pmp= number of corneal transplantations per million people; Waiting= number of individuals on the waiting list in December of each year for the procedure; Waiting/pmp= number of individuals on the waiting list in December of each year for the procedure per million people; DCT= efficacy of meeting the demand for corneal transplantation in percentage; Centers= number of corneal transplantation centers; Teams= number of corneal transplantation teams; Prod= productivity of corneal transplantation teams; NA= not available.

in the 16 years investigated. The waiting list for the procedure decreased from 23,549 (123 pmp) in 2008 to 12,865 (62.4 pmp) in 2016, which was approximately 45.4% in 8 years ($p<0.001$). The DCT increased by 50.7% (from 35.3% in 2008 to 53.2% in 2016; $p<0.001$). There was an 11-fold increase in the number of CT centers (from 32 to 356) and a 2.5-fold increase in the number of CT teams (from 276 to 688). CT teams performed an average of 19 CTs per year.

Table 2 shows the number of CTs, as well as the number and productivity of CT teams, per year in Brazilian regions from 2001 to 2016. All Brazilian regions experienced a gradual increase in the number of CTs over a period of 16 years. The number of CT teams doubled on average in all the regions, except for the southeast region where the growth tripled over this period. The average productivity of CT teams remained stable in the midwestern (23) and southern (30) regions, but it increased between 2001 and 2016 in the northern (from 11 to 25) and northeastern (from 10 to 32) regions and decreased in the southeastern region (from 25 to 16) after 16 years.

Table 3 shows the number of CT pmp, waiting list for the procedure pmp, and DCT per year in Brazilian regions from 2001 to 2016. All the regions exhibited a gradual increase in the number of CT pmp after 16 years and a reduction in the waiting list after 9 years. DCT improved the most in the southern region, increasing nearly 4-fold (from 23.1% to 89.5%), while it remained stable in the southeastern region (average of 57.6%). In 2016, the northern, northeastern, and midwestern regions accounted for only 30.3%, 47.2%, and 57.7% of the demand, respectively.

Table 4 shows the summary for the variables evaluated: number of CT pmp, waiting list for the procedure pmp, productivity of CT teams, and DCT in Brazilian regions from 2001 to 2016. The average number of CT pmp ($p<0.001$) in the midwestern (86.3 pmp) and southeastern (77.3 pmp) regions was similar and higher than that in the southern region (65.8 pmp), which was higher than in the northeastern region (35.1 pmp). The northern region had the lowest mean value (16.9 pmp).

The midwestern region (158.6 pmp) had the highest mean number of individuals on the waiting list pmp ($p=0.028$) compared with other regions, which had similar values. The average productivity ($p<0.001$) in the southern region was the highest (30 CTs per team), followed by the midwestern (23 CTs) and northeastern (20.6 CTs) region, which had similar values. The southeastern (16.6 CTs) and northern (12.8 CTs) regions had the lowest average values. The mean DCT ($p<0.001$) in the southern and southeastern regions was the same (57.6%) and was

Table 2. Number of corneal transplantations, number of corneal transplantation teams, and productivity of corneal transplantation teams in Brazilian regions from 2001 to 2016

	Midwestern			Northern			Northeastern			Southern			Southeastern		
Year	Trans	Teams	Prod	Trans	Teams	Prod	Trans	Tams	Prod	Trans	Teams	Prod	Trans	Teams	Prod
2001	764	33	23	98	9	11	531	55	10	1166	36	32,4	3634	143	25
2002	788	38	21	151	14	11	831	73	11	1218	58	21,0	3568	343	10
2003	891	38	23	86	15	6	940	81	12	1217	65	18,7	4422	388	11
2004	1138	60	19	88	22	4	1186	87	14	1168	63	18,5	4814	413	12
2005	1215	59	21	117	22	5	1200	79	15	1333	58	23,0	6105	391	16
2006	1200	62	19	147	21	7	1275	80	16	1705	60	28,4	6055	399	15
2007	1062	53	20	187	21	9	1481	80	19	1771	53	33,4	6918	379	18
2008	1037	59	18	252	22	11	1813	96	19	1836	56	32,8	7887	385	20
2009	1091	49	22	230	25	9	2114	94	22	1968	57	34,5	7320	401	18
2010	990	51	19	276	22	13	1981	107	19	2007	66	30,4	7669	417	18
2011	1588	47	34	317	26	12	2654	89	30	2678	65	41,2	7601	422	18
2012	1794	57	31	486	25	20	3016	103	29	2353	70	33,6	7492	415	18
2013	1397	59	24	465	25	19	2896	98	30	2030	66	30,8	6977	416	17
2014	1395	62	23	475	22	22	2666	106	25	2248	69	32,6	6672	422	16
2015	1556	58	27	463	21	22	2624	97	27	2367	68	34,8	6783	427	16
2016	1491	60	25	576	23	25	3387	106	32	2326	68	34,2	6861	431	16

Trans= number of corneal transplantations; Teams= number of corneal transplantation teams; Prod= productivity of corneal transplantation teams.

superior to the values in the midwestern (42.6%) and northeastern (38.6%) regions, which were similar and superior to the northern region (22.6%).

DISCUSSION

The demand for CT has increased due to the population's greater knowledge about corneal diseases and the possibility of cure, greater accessibility to health services, development of less invasive and safer keratoplasty techniques, increasing number of ophthalmologists able to perform transplantations and treat complications, and better visual rehabilitation in the postoperative period[10-12,24-27].

Surgical techniques allowing for selective replacement of anterior and posterior pathologic corneal tissue while retaining the healthy parts of the cornea are currently the "state of the art" in CT[28,29]. Unfortunately, in Brazil, the legislative structure is not yet in place to allow eye banks to offer precut anterior and posterior corneal grafts[14].

The indications for CT are distinct across countries and depend on the socioeconomic and demographic conditions of each population[29-36]. The main indications described in the literature are keratoconus[33-35], infectious keratitis, post-infection corneal scars[17,24,32,37,38], and bullous keratopathy[29,30].

A study conducted by Sobrinho et al.[39] showed bullous keratopathy as the main indication for CT in the state of Pará (northern region of Brazil). It is believed that in regions where residents experience difficulties in accessing health services, the surgical indication is late and subsequent intumescent cataracts increase the difficulty of surgery and the number of intra- and postoperative complications, including bullous keratopathy[40]. However, this topic requires extensive and complex discussions, and for that, another article will be needed to discuss it in detail.

Studies conducted in other parts of Brazil, in Latin America, and in Europe revealed keratoconus as the first indication of CT[33-35]. Several other causes for keratoplasty have also been described in the literature, including leukoma, corneal ulcer, graft rejection/failure, descemetocele, trachoma, Fuchs' dystrophy, and congenital anomalies[32-41].

Brazil currently has the largest public organ and tissue transplant program in the world[15]. In 2016, there were 53 eye banks in operation in the country, 5 in the midwestern, 4 in the northern, 12 in the northeast, 14 in the south, and 18 in the southeastern regions[42].

Table 3. Number of corneal transplantations per million people, waiting list for the procedure per million people, and efficacy of meeting the demand for corneal transplantation in percentage in Brazilian regions from 2001 to 2016

	Midwestern			Northern			Northeastern			Southern			Southeastern		
Year	Trans/ pmp	Waiting/ pmp	DCT (%)	Trans/ pmp	Waiting/ pmp	DCT (%)	Trans/ pmp	Waiting/ pmp	DCT (%)	Trans/ pmp	Waiting/ pmp	DCT (%)	Trans/ pmp	Waiting/ pmp	DCT (%)
2001	63.1	NA	NA	7.2	NA	NA	10.7	NA	NA	45.4	NA	NA	48.5	NA	NA
2002	63.7	NA	NA	10.9	NA	NA	16.6	NA	NA	46.9	NA	NA	47.0	NA	NA
2003	70.7	NA	NA	6.1	NA	NA	18.5	NA	NA	46.3	NA	NA	57.6	NA	NA
2004	88.6	NA	NA	6.1	NA	NA	23.1	NA	NA	44.0	NA	NA	62.0	NA	NA
2005	92.8	NA	NA	7.9	NA	NA	23.1	NA	NA	49.7	NA	NA	77.8	NA	NA
2006	90.0	NA	NA	9.7	NA	NA	24.3	NA	NA	62.9	NA	NA	76.3	NA	NA
2007	78.2	NA	NA	12.2	NA	NA	27.9	NA	NA	64.7	NA	NA	86.3	NA	NA
2008	75.1	253.1	22.9	16.1	93.1	14.7	33.9	93.9	26.5	66.5	221.7	23.1	97.5	92.0	51.4
2009	77.6	313.4	19.9	14.4	101.2	12.5	39.1	116.5	25.1	70.6	158.2	30.9	89.6	86.2	51.0
2010	69.3	300.4	18.7	17.0	99.1	14.7	36.3	95.5	27.6	71.4	112.6	38.8	93.1	92.4	50.2
2011	109.3	168.5	39.3	19.2	77.3	19.9	48.3	72.7	39.9	94.5	100.7	48.4	91.5	84.1	52.1
2012	121.5	109.4	52.6	29.0	82.6	26.0	54.5	58.1	48.4	82.4	49.3	62.6	89.4	31.3	74.0
2013	93.2	61.9	60.1	27.4	61.9	30.7	51.9	53.8	49.1	70.5	31.3	69.2	82.6	32.2	71.9
2014	91.7	78.1	54.0	27.6	70.2	28.2	47.4	60.7	43.9	77.5	26.7	74.4	78.4	48.7	61.7
2015	100.8	72.5	58.1	26.5	74.3	26.3	46.4	71.7	39.3	81.0	18.1	81.7	79.1	66.2	54.4
2016	95.2	69.9	57.7	32.5	74.5	30.4	59.5	66.6	47.2	79.0	9.3	89.5	79.4	74.0	51.8

Trans/pmp= number of corneal transplantations per million people; Waiting/pmp= number of individuals on the waiting list in December of each year for the procedure per million people; DCT= efficacy of meeting the demand for corneal transplantation in percentage; NA= not available.

Table 4. Measures of number of corneal transplantations per million people, waiting list for the procedure per million people, productivity of corneal transplantation teams, and efficacy of meeting the demand for corneal transplantation in percentage in Brazilian regions from 2001 to 2016 in Brazil

	Mean	Standard deviation	Minimum	Maximum	1º quartile	Medium	3º quartile	n	p
Trans/pmp									<0.001
Northern	16.9[D]	9.1	6.1	32.5	8.4	15.3	27.2	16	
Northeastern	35.1[C]	15.0	10.7	59.5	23.1	35.1	48.1	16	
Southeastern	77.3[A]	15.6	47.0	97.5	65.6	79.3	89.6	16	
Southern	65.8[B]	15.5	44.0	94.5	47.6	68.5	78.6	16	
Midwestern	86.3[A]	16.4	63.1	121.5	71.8	89.3	94.7	16	
Waiting/pmp[1]									0.028
Northern	81.6[B]	13.5	61.9	101.2	72.3	77.3	96.1	9	
Northeastern	76.6[B]	20.9	53.8	116.5	59.4	71.7	94.7	9	
Southeastern	67.5[B]	24.5	31.3	92.4	40.5	74.0	89.1	9	
Southern	80.9[B]	73.0	9.3	221.7	22.4	49.3	135.4	9	
Midwestern	158.6[A]	104.1	61.9	313.4	71.2	109.4	276.8	9	
Productivity									<0.001
Northern	12.8[C]	6.6	4.0	25.0	7.5	11.2	19.2	16	
Northeastern	20.6[B]	7.5	9.7	32.0	14.0	18.7	28.8	16	
Southeastern	16.6[C]	3.7	10.4	25.4	15.3	16.4	18.3	16	
Southern	30.0[A]	6.5	18.5	41.2	24.4	32.5	34.1	16	
Midwestern	23.0[B]	4.5	17.6	33.8	19.6	22.4	24.5	16	
DCT (%)[1]									<0.001
Northern	22.6[C]	7.2	12.5	30.7	14.7	26.0	29.3	9	
Northeastern	38.6[B]	9.7	25.1	49.1	27.1	39.9	47.8	9	
Southeastern	57.6[A]	9.4	50.2	74.0	51.2	52.1	66.8	9	
Southern	57.6[A]	23.4	23.1	89.5	34.9	62.6	78.1	9	
Midwestern	42.6[B]	17.6	18.7	60.1	21.4	52.6	57.9	9	

p value= descriptive level of ANOVA.
(A), (B), (C), and (D) present distinct means according to Duncan's multiple comparisons.
[1]= Data made available from 2008.
Trans/pmp= number of corneal transplantations per million people; Waiting/pmp= number of individuals on the waiting list in December of each year for the procedure per million people; p= productivity of corneal transplantation teams; DCT= efficacy of meeting the demand for corneal transplantation in percentage; n= number of years analyzed.

The National Organ and Tissue Transplantation Policy is based on laws that guarantee free donation, beneficence toward recipients, and non-maleficence toward donors[43]. Notification of potential donors is required and should be reported to the Organ Notification, Collection and Distribution Unit (CNCDO), as well as to the eye bank operating in the region. According to the Ministry of Health, the waiting list for transplants is unique in each state of Brazil, and care is given in order of arrival, considering emergency criteria[43].

Brazilian law requires family consent for the removal of organs and tissues for transplant[44]. A recent modification in the legislation[45] enables authorization of the donation by family members up to the second degree.

Considering the number of cornea pmp donated in 2016, Brazil had a rate of 146.8 pmp, ahead of other developing countries such as Costa Rica (35.1 pmp), Mexico (26.9 pmp), Uruguay (24.7 pmp), Ecuador (16.8 pmp), Paraguay (12.8 pmp), and Chile (10.1 pmp)[46].

Table 1 shows that the number of corneal transplants performed in Brazil increased from 6,193 in 2001 (35.2 pmp) to 14,641 in 2016 (71.0 pmp), an increase of approximately 136% over 16 years ($p<0.001$). The waiting list for the procedure decreased from 23,549 (123 pmp) in 2008 to 12,865 (62.4 pmp) in 2016, approximately 45.4% in 8 years ($p<0.001$).

According to the Brazilian Association of Organ Transplants (ABTO), the estimated annual need for keratoplasty in 2016 was 18,401 transplants (90 pmp)[47]. According to the data shown in table 1, a total of 14,641 transplants (71.0 pmp) were performed in 2016, approximately 20.5% (3,760) less than the ideal number for the country.

The results showed that the country met 35.3% of the CT (DCT) demand in 2008 and 53.2% in 2016 (Table 1). However, despite the increase of 50.7% over the years, the DCT in Brazil remains low, which contributed to the high number of patients on the waiting list for CT in 2016 (12,865 patients - 62.4 pmp).

In 2001, the Ministry of Health established the National Program for the Implementation of Tissue Eye Banks, whose purpose was to increase the collection of corneas, shorten the time spent by recipients on the waiting list, and significantly increase the number of CTs performed[48].

The effect of this measure can be observed in the data presented in this study, as the number of CT centers and CT teams increased 11 folds (from 32 to 356) and 2.5 folds (from 276 to 688), respectively (Table 1). The productivity of the CT teams remained constant over the years, with an annual average of 19 CTs per team over 16 years (Table 1).

The obstacle to further progress is not the low number of CTs or the productivity of CT teams, but is probably related to the number of corneal donations, which has yet to meet the needs of the Brazilian population.

Studies emphasize the importance of greater conversion of potential donors to effective donors and, consequently, increased rates of CT, in order to ensure adequate population assistance[49,50]. Prolonged time on a waiting list has a negative impact on biopsychosocial well-being, cure probabilities, the nature and extent of sequelae in patients, family members, and society[14,51].

The waiting time for CT has been described in the literature for some Brazilian states: in Pará, most patients waited 1 to 3 years for CT[39], while in the states of Pernambuco[37] and São Paulo[52], the wait was approximately 4 months.

In some Brazilian states and regions, recruitment teams concentrate their efforts on obtaining the cornea of multiple organ donors, taking action following brain deaths, and mobilization in cases of cardiorespiratory arrest, which are an important source of corneal donations. This is an important measure that would help reduce the waiting lists for CT in the country.

Brazilian law establishes[43] a legal requirement to collect eye tissues only within 6 hours after death or 24 hours if the entire body is kept in a cold room. The protocol observed by the Eye Bank Association of America[53] does not establish a period for collecting corneas after death. Rather, it states that ice packs should be used in the orbital area over the eyelids to extend the time limit for enucleation, thus attempting to reduce damage to eye tissues by toxins that form naturally after death. Because of the legal time limit for collecting corneas in Brazil, many corneas are rejected for donation[14].

With regard to organ and tissue donation, several reasons for family refusal have been documented in the literature, including religious motivations, bureaucracy, lack of credibility of the health system, lack of knowledge of the concept of brain death, and fear of negligent medical treatment to speed up donation[14,53-61]. Studies have shown that the information on CT provided to the population, medical students, physicians, and health professionals remains insufficient[42,55,62-65].

Therefore, if assisting health professionals and staff involved in the identification of potential donors and family interviews were adequately trained and qualified, the number of tissue donated would likely increase, effectively reducing the waiting lists for CT in the country.

Brazil is a country of continental dimensions with important social, cultural, and economic diversity between regions, which influence the quality of health services provided to the society. Research has shown that although the number of CTs in Brazil has increased over the years, regional differences still need to be resolved. The large number of CTs concentrated in a few states in comparison with other populous states in Brazil is worthy of note[14,66].

Tables 2 and 3 show that the number of CTs performed in the northern and northeast regions increased 5 folds in 16 years. However, in 2016, this number accounted for only 4% (576 CTs – 32.5 pmp) and 23% (3,387 CTs - 59.5 pmp) of the country's CT, respectively, while the southeast region accounted for 47% (6,861 CTs - 79.4 pmp) that year. The number of CTs reached a peak of 1,794 (121.5 pmp) in 2012 in the midwestern region, but it has been declining since, reaching 1,491 CT (95.2 pmp) in 2016, the highest value found in Brazil that year.

Nonetheless, all Brazilian regions showed a gradual increase in the number of CT pmp after 16 years (Table 3). Additionally, during the period under study, the average number of CT pmp ($p<0.001$) in the midwestern (86.3 pmp) and southeastern (77.3 pmp) regions were similar and higher than in the southern region (65.8 pmp), which in turn was higher than in the northeastern region (35.1 pmp). The northern region (16.9 pmp) had the lowest mean value (Table 4).

The number of CT teams doubled on average in all regions except in the southeast, where growth tripled over the same period (Table 2). However, the distribution of teams in Brazil is heterogeneous. In 2016, 63% (431) of the CT teams were located in the southeastern

region and 13% (106) were located in the northeastern region. The southern and midwestern regions had less than 10% each of the teams registered in the country, and there were only 3% teams registered in the country in the norther region (23).

Table 2 shows that the productivity of the CT teams remained stable over the 16 years evaluated in the midwestern (23) and southern (30) regions, but it increased between 2001 and 2016 in the northern (from 11 to 25) and northeast (from 10 to 32) regions and decreased in the southeastern region (from 25 to 16). The latter was due to the high number of teams registered in the region in 2016 (431). During the period under study, the average productivity ($p<0.001$) was highest in the southern region (30 CTs per team), followed by the midwestern (23 CTs) and northeastern (20.6 CTs) regions, which were similar. The southeastern (16.6 CTs) and northern (12.8 CTs) regions had the lowest average values (Table 4).

It should be noted that the reduced number of CT teams may indirectly represent a lower number of ophthalmologists capable of diagnosing and treating severe corneal diseases. This would hamper population access to specialized medical care and reduce the number of CT indications, thus falsifying the number of patients on the waiting list.

Kara-Junior et al.[6] described the difficulty of access to the waiting list, stating that 50% of the patients, especially those with low income and an indication for CT, did not join the queue because they were not correctly oriented, did not understand the information, and did not present socioeconomic conditions necessary to enable treatment and to register effectively on the waiting list for CT.

Table 3 shows that the DCT increased in the southern region, which had a nearly 4-fold increase between 2008 (23.1%) and 2016 (89.5%). The DCT for the southeast region peaked in 2012 (74%) and remained stable afterward (average of 57.6%). In 2016, the northern, northeastern, and midwestern regions accounted for only 30.3%, 47.2%, and 57.7% of the demand, respectively. Table 4 shows that the mean DCT ($p<0.001$) in the southern and southeastern regions was the same (57.6%) and superior to the midwestern (42.6%) and northeastern (38.6%) regions, which were similar and superior to the northern region (22.6%).

All the regions of Brazil had a reduction in the waiting list after 9 years, but the highlight was the southern (6.121 patients [221.1 pmp] to 273 patients [9.3 pmp]) and midwestern (3,497 patients [253.1 pmp] to 1,095 patients [69.9 pmp]) regions, which showed a significant decrease in the queue (Table 3). The number of patients in waiting lists decreased by approximately 1.3 folds in the northern (to 74.5 pmp), northeastern (93.9 to 66.6 pmp), and southeast (92 to 74 pmp) regions. In 2016, 6,388 (74 pmp) patients were awaiting CT in the southeast region, which was equivalent to 50% of the total number of patients in the waiting list in Brazil that year. The midwestern region (158.6 pmp) had the highest mean number of individuals on the waiting list pmp ($p=0.028$) compared with the other regions, which were similar to each other (Table 4).

This finding probably indicates that patients are migrating from other regions to the state of Goiás, São Paulo, and Federal District, which have a more structured transplantation program and provide easier access to health services and treatment to the population compared to other Brazilian states.

According to a study by Almeida et al.[39], states in the northern and northeastern regions of Brazil experience difficulty with temporary contract regimes, high turnover of staff in centers, logistical problems, and lack of cooperation between municipal and state governments, often motivated by political differences. Thus, difficulties with corneal donation and transplants identified in these regions are consequences of recent and poorly structured transplant programs, lack of qualified professionals, and limited resources for infrastructure investment, resulting in low rates of notification of potential donors, corneal uptake, and CTs performed[47].

These regions and states with lower CT rates in Brazil require a greater number of Intra-Hospital Commission on Organ and Transplant Tissue Donation (CIHDOTT) and Organ and Tissue Procurement Organizations that are capable of identifying potential donors, conducting a proper family interview, and increasing the number of accepted donations of organs and tissues.

The greatest number of CTs is concentrated in the southeastern, midwestern, and southern regions of Brazil, where programs are better structured, are more established, receive support from the local government, and have better prepared medical teams, all of which clearly contribute to facilitating access to health services and improving care for the population[47].

The data disclosed by SNT show that Brazil has been improving its capacity to perform CTs in the past 16 years, although this improvement varies across regions. However, it is necessary to expand the resources provided in Brazilian law to reimburse eye banks, rather than the hospitals in which they are installed, for the proce-

dures performed. The resources allocated to banks must be sufficient to cover the costs of purchasing equipment, consumables, means of preservation, transport system, communication, hiring of human resources for 24-hour operation, and provision of quality service to society.

It is also essential to strengthen SNT and to standardize the data made available to the public, health professionals, ophthalmology society, and the government to ensure proper reporting of annual variables so that more detailed research can be conducted in Brazil. This would make it possible to improve the capacity to meet the annual demand for corneal transplants, drastically reducing the time and number of patients in corneal transplant waiting lists.

This study also emphasizes the importance of increasing the awareness of the Brazilian population through information about CT. It is necessary to act in the media to publicize and promote the donation of organs and tissues, emphasizing the capacity of this humanitarian act to save and improve the quality of life for the patients treated, their families, and society in general.

In addition, we reinforce the importance of developing new studies in the Brazilian regions and states in order to create a detailed national overview of corneal transplants, identify local difficulties, and suggest specific solutions capable of overcoming social, cultural, and economic barriers to CT progress in the donation, capture, storage, and distribution of corneas in Brazil and Brazilian regions.

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