

Outcomes of cataract surgery with/without vitrectomy in patients with pars planitis and immunosuppressive therapy

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Abstract

Background The purpose of this study was to evaluate the characteristics and outcomes of cataract surgery with/without vitrectomy in patients with pars planitis who received immunosuppressive therapy.

Methods This was a retrospective case series, single-center study. Twenty-two patients with pars planitis who received immunosuppressive therapy were included, with a median age at presentation of 9.5 years, having had cataract surgery. The following data was collected: age at presentation and at cataract surgery, time of follow-up, best-corrected visual acuity (BCVA) before the surgery and at 1 week, 1 and 6 months after the procedure, immunosuppressive therapy, complications and causes for failed visual improvement. The variables associated with an improvement in visual acuity were evaluated.

Results All patients had phacoemulsification with intraocular lens implantation. The most common immunosuppressive therapy used for the patients was methotrexate in nine patients (40.9%). The BCVA improved from a median of 20/400 to 20/100 after 6 months of follow-up ($p = 0.0005$); 14 patients (63.6%) improved two lines of vision or more. No significant risk factors were found for the association with improvement in visual acuity after the surgery. No improvement in visual

acuity was attributed to posterior segment manifestations or amblyopia; the most common complication was posterior capsule opacification in 11 eyes (50%). The median follow-up after the surgery was 32 months.

Conclusion Phacoemulsification was the procedure for all the patients. Visual acuity improved in patients with pars planitis treated with immunosuppressive drugs who underwent cataract surgery, except for the patients with posterior segment complications or amblyopia.

Keywords Pars planitis · Immunosuppressive therapy · Cataract surgery · Phacoemulsification · Visual outcomes

Introduction

Pars planitis is an intermediate uveitis with snowbanking and snowball formation in the absence of infection or an associated disease, with cataract formation as a common complication [1, 2]. Children with uveitis develop cataract in 40 to 60% of cases; cataract formation comes from persistent chronic inflammation in close proximity to the lens and from the prolonged corticosteroid exposure [3, 4]. It is generally accepted that the eye should be free of inflammation for at least 3 months before surgery, and the surgical treatment remains challenging.

Treatment for moderate to severe inflammation requires the use of non-steroidal immunosuppressants to achieve control as well to minimize the risk of complications associated with the prolonged use of systemic steroids; it is estimated that 15 to 25% of patients with pars planitis will require treatment with immunosuppressants [5]. The use of immunomodulatory drugs in controlling inflammation may be beneficial in cataract surgery among this population.

The purpose of this study is to evaluate the characteristics and outcomes of cataract surgery with or without vitrectomy

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in patients with pars planitis who received immunosuppressive therapy.

Materials and methods

This is an observational and retrospective clinical study. We reviewed the clinical records between November 2001 and February 2014 of 378 patients with pars planitis, and from the 98 that underwent cataract surgery, we included the patients with immunosuppressive therapy. Inclusion criteria were chronic pars planitis with control of inflammation ($<0.5+$ cells in anterior chamber or vitreous body) for at least 3 months before surgery, reduced visual acuity ($<20/50$ Snellen or 0.4 logMAR) mainly due to cataract or the presence of cataract that would preclude posterior segment evaluation, phacoemulsification with primary intraocular lens (IOL) implantation, use of immunosuppressive therapy before cataract surgery and follow up of at least 6 months. Exclusion criteria were patients who had cataract surgery in other institution, patients with unspecified immunosuppressive therapy and incomplete medical records.

Clinical diagnosis of pars planitis was made as follows: presence of an intermediate uveitis with vitreous cellularity and snowbanking or snowballs in at least one eye in the absence of an associated infection (confirmed by laboratory) or underlying systemic illness. Treatment of the patients with pars planitis followed a step ladder approach according to the severity of the disease, with topical or regional steroids with paraocular drug administration, topical or systemic nonsteroidal anti-inflammatory drugs (NSAIDs), and oral systemic steroids calculated 1 mg/kg/day.

The systemic immunosuppressive therapy was considered in the following clinical settings: (1.) lack of response to the initial treatment, (2.) advanced disease, (3.) insufficient effect of systemic steroids, (4.) adverse effects of steroids and (5.) high doses or prolonged steroid use [5]. The standardized doses used for the immunosuppressive drugs were methotrexate 2.5 – 15 mg/week, azathioprine 1 – 3 mg/kg and cyclophosphamide 1 – 3 mg/kg/day; however, dosifications were individualized in some cases [6]. Systemic infections were ruled out in all cases prior to initiating immunosuppressive therapy.

Cataract surgery was considered when patients developed a significant decrease in visual acuity or associated symptoms. As part of the treatment protocol for cataract surgery, all patients underwent complete medical history, recording best-corrected visual acuity (BCVA), biomicroscopy of the anterior segment, and posterior pole if it was possible according to media transparency. All patients had ultrasound measurement of axial length and calculation of IOL, usually with the SRK II formula. The surgeries were performed under general anesthesia for the pediatric patients and with peribulbar anesthesia for the rest of patients. Phacoemulsification was the procedure. In all cases a 2.8 mm clear corneal incision was made at 130° ,

pupils were managed with synechiolysis and iris hooks or iris retractors, if needed. Care was taken to create a 5.0 to 6.0 mm continuous curvilinear capsulorhexis previous staining of the capsular bag with trypan blue and hydrodissection followed by phacoemulsification or phacoaspiration. IOLs were acrylic hydrophobic in all cases (Alcon Acrysoft SN60WF, 13.0 mm), implanted in the bag and for only two patients in sulcus (Alcon Acrysoft MN60MA, 13.0 mm). Finally, closure of clear corneal incision was done with 10 – 0 nylon suture. If posterior capsular fibrosis was present, posterior capsulotomy and automated anterior vitrectomy were performed and in cases with significant vitreous opacities a pars plana vitrectomy was made by a vitreo-retinal surgeon; with remotion of an important amount of vitreous with the induction of a posterior hyaloid detachment using either 20 or 23 G. All patients received a periocular injection of betamethasone (Diprospan, Schering Plough) at the end of the surgery. Postoperative management consisted in the application of topical antibiotics with a second (Sophixin, Sophia Labs) or fourth generation fluoroquinolone (Vigamoxi, Alcon), a course of topical steroid drops with prednisolone acetate 1% (Prednefrin, Allergan) in a tapering regimen according to the postoperative inflammation, and hypotensive drugs if needed. Ocular hypertension was defined as an intraocular pressure higher than 21 mmHg. Postoperative follow-up was registered at 1 week, 1 month, 6 months and final follow-up.

Approved informed consent was obtained from all patients (or patients' caretakers in the case of minors) undergoing immunosuppressive therapy and cataract surgery. The data acquisition, study design and methodology were carried out with the approval of the Ethics Committee and Research Board of the Instituto de Oftalmologia Conde de Valenciana. The study was in adherence to the guidelines of the Declaration of Helsinki.

Statistical analysis

We assessed the following variables: age at presentation, age at cataract surgery, time of follow-up, BCVA before the surgery and at 1 week, 1 month and 6 months after the procedure and at the final follow-up, immunosuppressive therapy, surgical and postoperative complications and causes for failed visual improvement. BCVA was analyzed in the logMAR units. Categorical variables were evaluated using percentages and numerical variables were assessed using measures of central tendency for non-parametric distribution. Comparisons between groups of patients with and without improvement in BCVA after surgery were performed with Student's *t*-test for continuous variables and with Fisher's exact test for categorical variables. The comparison of preoperative BCVA and after 6 months was performed with a paired *t*-test. Spearman's correlation between BCVA before and after surgery was used. Through a robust multiple logistic regression analysis, the variables associated with an improvement in

visual acuity after the surgery were evaluated, obtaining the odds ratio (OR) and 95% confidence interval (95% CI). Analysis was done using STATA 13.1 (STATA Corp, College Station, TX, USA).

Results

Patient characteristics

Of the 378 patients with pars planitis in the records, 22 met the inclusion criteria; a flow chart showing the inclusion to the study is illustrated in Fig. 1.

The median age at presentation was 9.5 years (range 3 to 22 years); 17 patients (77.3%) were male and five (27.2%) were female. All patients had bilateral pars planitis, but only one eye had significant cataract and was considered for surgery, which was the right eye in ten patients (45.4%) and the left eye in 12 patients (54.6%).

Cataract surgery

The median age at the moment of cataract surgery was 10.5 years (range 7 to 25 years). All the patients had phacoemulsification, with IOL implantation in the capsular bag in 20 patients (90.9%) and two patients (9.1%) with implantation in the sulcus (Fig. 2). In 15 patients (68.2%) vitrectomy was performed; anterior vitrectomy in six patients (40%), pars plana vitrectomy in nine patients (60%) and no vitrectomy for seven patients (31.8%). The eyes with pars plana vitrectomy and without vitrectomy did not undergo primary posterior capsulotomy. The median follow-up after the surgery was 32 months (range 6 to 122 months).

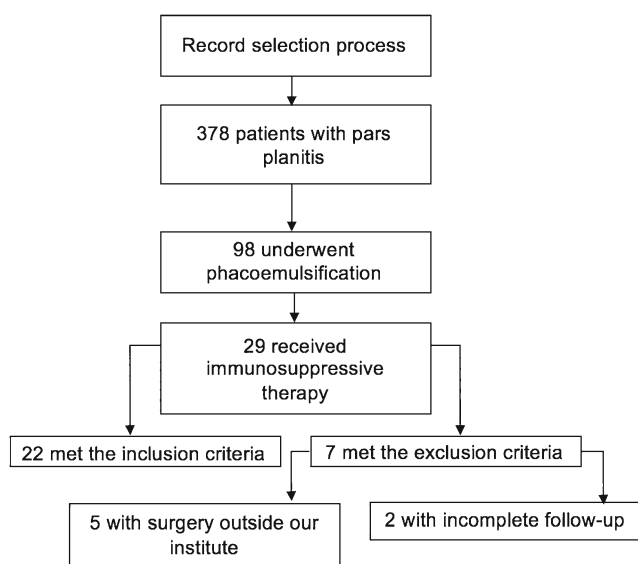


Fig. 1 Flow chart of the data-selection process

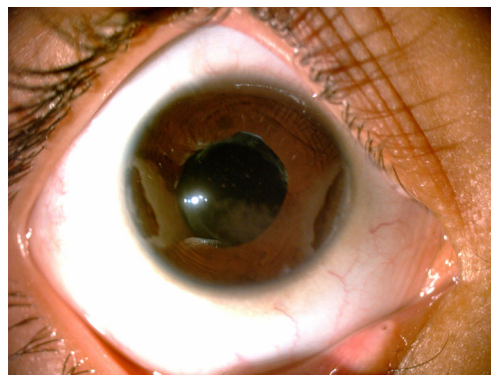


Fig. 2 Nine-year-old male patient with pars planitis under immunosuppressive therapy. An intraocular lens is evident after his cataract surgery, with central band keratopathy and pigmented keratic precipitates

Immunosuppressive therapy

The immunosuppressive therapy used for the patients were methotrexate alone in nine patients (40.9%), azathioprine in four (18.2%), cyclophosphamide in two (9.1%) and seven patients (31.8%) requiring a combination of drugs which were methotrexate and azathioprine for all of them. The median time using the immunosuppressants before surgery was 9.5 months (3.5 to 50.5 months). Therapy included oral corticosteroids as well in 15 patients (68.1%) before cataract surgery. The corticosteroids used were deflazacort in ten patients (66.7%) and prednisone in five patients (33.3%).

Adverse effects were observed in six patients (27.2%). In one case (4.5%) there was only lightheadedness, two cases had abnormal liver function tests, two patients presented with leukopenia, and one patient hematuria, with all of them normalized after reducing the dose of immunosuppressants. The two cases (9.1%) of abnormal liver function tests were present in the group of combined methotrexate and azathioprine, and the rest of adverse effects were present in the methotrexate group.

Visual outcome

The BCVA improved from a median of 20/400 (logMAR 1.3) to 20/100 (0.7 logMAR) after 6 months of follow-up ($p = 0.0005$); 14 patients (63.6%) improved two lines of vision or more, another two patients (9.1%) gained one line, another four patients (18.2%) remained with the same BCVA and two patients (9.1%) lost BCVA due to tractional retinal detachment and epiretinal membrane, respectively. The characteristics of each patient are presented in Table 1.

A comparison between groups of patients with and without improvement in visual acuity after surgery did not find a statistical significance in age at presentation ($p = 0.688$), age at surgery ($p = 0.736$) or gender ($p = 0.419$). Also, there was no correlation between difference in BCVA before and after the

Table 1 Characteristics and visual outcomes of patients with pars planitis, immunosuppressive therapy and Phacoemulsification and intraocular lens implantation

Visual Acuity										
Patient/ sex	Age in years at presentation/ surgery	Vitrectomy	Pre-operative LogMAR	1 month LogMAR	6 months LogMAR	Final LogMAR	Change in lines* [#]	Time with immunosuppressor (months)	Time without inflammation before surgery (months)	Immunosuppressor used
1/F	3/8	Anterior	1.82	1.00	0.30	1.82	0	3.8	4	MTX 2.5 mg/week
2/M	3/8	Anterior	HM	1.82	2.00	2.00	1	3.5	6	CFM 25 mg/day
3/M	5/8	PP	HM	HM	2.00	HM	0	50.5	6	MTX 7.5 mg/week AZT 50 mg/day
4/M	5/7	PP	1.30	0.60	0.40	0.18	10	14.5	13	MTX 5 mg/week AZT 50 mg/day
5/M	6/7	No	1.30	1.30	1.30	0.70	5	10.1	3	AZT 50 mg/day
6/M	6/10	PP	1.30	0.30	0.48	0.30	9	25.5	10	CFM 25 mg/day
7/M	6/7	Anterior	2	0.30	0.30	1.00	9	7.1	5	AZT 50 mg/day
8/M	7/9	Anterior	HM	0.70	0.60	0.10	19	19.0	12	MTX 10 mg/week AZT 50 mg/day
9/F	8/10	No	1.60	0.40	1.80	1.00	5	29.0	9	MTX 2.5 mg/week
10/M	10/11	Anterior	1.30	1.00	0.70	0.60	6	7.7	7	MTX 7.5 mg/week
11/F	11/12	PP	1.30	1.00	0.70	LP	-6	4.6	5	AZT 100 mg/day
12/M	11/13	PP	1.80	0.70	1.80	0.00	17	15.2	12	MTX 10 mg/week AZT 100 mg/day
13/M	11/12	PP	0.48	0.60	0.30	0.60	-2	12.5	5	MTX 12.5 mg /AZT 50 mg/day
14/M	11/11	No	2	1.30	1.30	1.00	9	7.9	4	MTX 7.5 mg/week
15/M	15/21	No	1.00	0.40	0.30	1.00	0	5.9	7	MTX 12.5 mg/week
16/F	20/29	PP	1.00	0.30	0.18	0.40	5	17.2	7	MTX 7.5 mg/week AZT 50 mg/day
17/M	20/20	No	1.00	1.00	0.54	1.00	0	3.5	4	MTX 5 mg/week
18/M	22/25	No	2	0.18	0.10	0.48	14	8.8	7	MTX 2.5 mg/week
19/M	9/10	PP	1.30	0.70	0.70	0.70	5	4.9	3	MTX 5 mg/week
20/M	15/21	No	1.30	0.70	1.00	1.00	3	8.2	5	AZT 50 mg/day
21/F	11/14	PP	0.70	1.00	0.70	0.54	2	20.8	8	MTX 10 mg/week
22/M	6/7	Anterior	HM	2.00	2.00	2.00	1	10.8	6	MTX 12.5 mg/week AZT 50 mg/day

*Change in lines in Snellen chart

PP Pars plana, MTX methotrexate, AZT azathioprine, CFM cyclophosphamide, HM Hand motion, LP Light Perception

surgery with age at surgery ($p = 0.249$) and time with immunosuppressive therapy before surgery ($p = 0.300$).

No improvement in visual acuity was attributed to posterior segment manifestations or amblyopia. Reasons for failing improvement in our study are shown in Table 2 for each patient. The most common complication was decreasing BCVA for posterior capsule opacification in 11 eyes (50%), epiretinal membrane in eight (36.2%), anterior capsule fibrosis in three (13.6%), central band keratopathy in two (9.1%), two cases of chronic angle closure glaucoma (9.1%), two cases of cystoid macular edema (9.1%) and a case of pupillary membrane (4.5%). In those patients with no complications reported and visual acuity worse than 20/20 (logMAR 0), patients 4, 6, 8, 16 and 18, we concluded by the age at surgery that they developed some degree of amblyopia (5 patients, 22.7%).

In a logistic regression analysis, after adjustment by age at the moment of cataract surgery and time of immunosuppressive medication before surgery, there was no difference on having visual improvement between those that received multiple immunosuppressive medications compared to those receiving only one drug was observed.

Table 2 Complications found at the last visit at final follow-up

Patient/ Age at surgery	Final BCVA	Reason for final BCVA <20/40 (0.30 logMAR)
1/8	1.82	Central band keratopathy
2/8	2.00	Central band keratopathy, ERM, previous tractional retinal detachment partially involving macula
3/8	HM	Tractional ERM
4/7	0.18	None
5/7	0.70	PCO, Pupillary membrane
6/10	0.30	None
7/7	1.00	ERM
8/9	0.10	None
9/10	1.00	Anterior capsule fibrosis
10/11	0.60	PCO, ERM
11/12	LP	PCO, chronic angle closure glaucoma
12/13	0.00	None
13/12	0.60	PCO, CME, ERM
14/11	1.00	PCO, ERM
15/21	1.00	PCO, ERM
16/29	0.40	None
17/20	1.00	PCO, ERM
18/25	0.48	None
19/10	0.70	PCO, CME
20/21	1.00	Anterior capsule fibrosis, PCO
21/14	0.54	Anterior capsule fibrosis, PCO
22/7	2.00	PCO, chronic angle closure glaucoma

PCO posterior capsule opacification, ERM epiretinal membrane, CME cystoid macular edema

Discussion

Pars planitis is a chronic ocular inflammatory disease, more common in young males and with cataract formation as a common complication and other factors limiting visual acuity [7]. Both the inflammatory disease and use of corticosteroids, whether topical or systemic, may induce cataract formation. In a study based on a cohort of 148 children with uveitis, cataract could be predicted to occur at a rate of 0.16 events per patient-year follow-up [8]. The incidence of cataract in pars planitis is found to be as high as 57% [3]. In our previous series of patients with pars planitis and immunosuppressive therapy, cataract was reported in 52.1% of cases [5].

Cataract surgery in those patients at pediatric ages is indicated if visual acuity is decreased or if visual deprivation is producing strabismus [4]. Unilateral cataracts may need earlier surgery in children at risk of developing amblyopia, and removal of dense cataract is also indicated to improve examination of posterior segment [9]. Although extracapsular cataract extraction in selected patients have shown visual improvement, most surgeons with expertise in uveitis perform phacoemulsification with in-the-bag IOL implantation in uveitic eyes with cataract with or without vitrectomy; the advantages of phacoemulsification include a small incision, short surgical time, less trauma to ocular tissues and minimal blood-aqueous barrier breakdown [10–12]. The outcome of surgery depends upon several factors like patient selection, proper preoperative medical management and meticulous surgery [13]. Many factors can contribute to the difficulty of the surgery such as band keratopathy and corneal deposits which can render poor visibility; peripheral anterior and posterior synechiae, pupillary membranes and fibrosis can impair surgical access; and long-standing inflammation may compromise the integrity of the capsule and zonule [14].

While previous studies compared IOL versus no IOL implantation in chronic iridocyclitis or pars planitis without statistical difference in visual acuity results at 1 year between the two groups, the reported success rate of cataract surgery with IOL implantation combined with vitrectomy is about 60% of patients reaching 20/40 (0.3 logMAR) of BCVA [15, 16]. Some authors agree that primary IOL implantation in pediatric uveitis cataract surgery can be associated with good long-term outcomes and should not be considered an absolute contraindication [17, 18]. Ganesh and colleagues analyzed the outcome of phacoemulsification with IOL implantation in 100 eyes with intermediate uveitis; in this study 91% of eyes showed a favorable visual outcome at an average follow-up of 19.6 months [11]. Uveitic eyes do have an increased risk for deposition of debris on the IOL [19]. The presence of an IOL can stimulate ocular inflammation and serve as a scaffold for the accumulation of inflammatory cells and debris, with the subsequent development of a fibrotic membrane [9]. Despite these complications, it has been shown that visual acuity in

patients with pars planitis can be improved after phacoemulsification with IOL implantation [11, 20]. In a review of types of IOLs for cataract surgery in eyes with uveitis, hydrophobic lenses are preferred over poly (methyl methacrylate) and silicone lenses, but hydrophilic IOLs achieved higher uveal compatibility [21]. Hydrophobic acrylic lenses were used for our patients, because it has been proven that they reduce the size of incision and may have satisfactory results in patients with uveitis [22].

To avoid the side effects of long-term corticosteroids, the role of immunomodulatory drugs for controlling inflammation has gained favor. High doses or prolonged use of steroids are associated with multiple systemic adverse effects including Cushing's syndrome, delayed growth in children, gastrointestinal symptoms, obesity, hyperglycemia, hyperlipidemia, asthenia, hypocalcaemia and skin disorders [5]. If the patient's disease worsens or if there is no response after 2 to 4 weeks, an immunosuppressive agent should be added [6]. Methotrexate was the preferred drug in our patients due to its safety profile and easy administration, and even when most of the adverse events related to immunosuppression were present in the methotrexate group, all of them were considered mild [5]. It is important to control ocular inflammation before surgery; complete quiescence of inflammation for at least 3 months is usually recommended [4, 14, 23].

Previous studies have reported an improvement of 20/40 (logMAR 0.3) or better in 69% of eyes with quiet or mostly quiet intermediate uveitis preoperatively [24]. We report only four (18.2%) of 22 patients approaching 20/40 (logMAR 0.3) of BCVA after surgery, which is a lower rate compared with other studies [11, 24, 25]. This can be explained as the need of immunosuppressive therapy usually correlates with patients with more severe disease, and already more preoperative complications. Also, our institution is an ophthalmology referral center, receiving patients with longer delay for diagnosis and treatment. In the other hand, compared with studies that reported an improvement of BCVA of 2 lines of Snellen from 60% to 79%, we had similar results (64%) [11, 16, 25]. Most studies had presented outcomes of cataract surgery in older patients, old enough to exclude amblyopia as a mayor cause of poor visual improvement. In accordance with our study, the most common complication reported in the literature is posterior capsular opacification [18]. Macular edema is a major complication following surgery in pars planitis and an important cause of poor vision in other series [11, 20, 23]. Acute intraocular inflammation, posterior synechiae and glaucoma seem to be other major postoperative complications [4].

Our study did not find specific significant risk factors for the lack of improvement in visual acuity after cataract surgery. A randomized clinical trial may give more information about the treatment of patients with pars planitis, the need of immunosuppression and cataract surgery. Meanwhile, the decision to take those complicated patients to surgery must be

individualized, and the appropriate time of previous immunosuppression is still debated. There are some weaknesses in our study. A retrospective analysis has the possibility of systematic bias relating to the selection of patients and loss of follow-up. The second weakness is the small sample size. Additionally, we did not include a group without immunosuppressive therapy to perform comparisons in outcomes.

In conclusion, this study reports the outcomes of cataract surgery with/without vitrectomy in patients with pars planitis and immunosuppressive therapy. Phacoemulsification was the procedure for all the patients. Immunosuppressants were added to systemic corticosteroids to control ocular inflammation and continued after the surgery. Visual acuity improved in patients with pars planitis treated with immunosuppressive drugs who underwent cataract surgery, except for the patients with posterior segment complications or amblyopia for delay in presentation.

Contributors Design of the study: TAG, JCSO and MPS. Conduct of the study: TAG. Collection and management of the data: TAG, JCSO and AJC. Analysis and interpretation of the data: TAG, JCSO, AJC and MPS. Preparation of the manuscript: TAG, JCSO, AJC and MPS. Review and approval of the manuscript: TAG, JCSO, AJC and MPS.

Compliance with ethical standards

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Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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