• Review Article •

Intraocular pressure measurement in keratoconus: a narrative review

Rafael Vidal Merola[1,2], *Sebastião Cronemberger*[2]

[1]Faculty of Medicine, Professor Antônio Carlos University Centre, UNIPAC, Juiz de Fora 36048-000, State of Minas Gerais, Brazil

[2]Nassim Calixto Glaucoma Service of São Geraldo Eye Hospital, Clinic Hospital, Federal University of Minas Gerais, Belo Horizonte 30130-100, State of Minas Gerais, Brazil

Correspondence to: Rafael Vidal Merola. Rua Santo Antônio, 416, apartamento 604, Centro, Juiz de Fora 36015-000, MG, Brazil. rafaelmerula@hotmail.com

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Abstract

● Accurate measurement of intraocular pressure (IOP) is essential for the diagnosis and treatment of glaucoma. Keratoconus (KC) is an ectatic corneal disease, which evolves with progressive non-inflammatory thinning and is characterized by irregular astigmatism, and alteration of corneal biomechanics. There are many doubts regarding the best method to measure IOP in patients with KC, and, as far as we know, there are no manometric studies in patients with KC. It seems that IOP measurements made by Goldmann applanation tonometry (GAT) probably underestimate the real values in patients with KC. With the aim of obtaining more accurate measurements of IOP in KC, new devices were developed such as dynamic contour tonometry (DCT), ocular response analyzer (ORA) and corneal visualization scheimpflug technology (Corvis-ST). Possibly, DCT, corneal-compensated IOP (IOPcc)-ORA, and biomechanical corrected IOP (bIOP)-Corvis-ST can reduce some inaccuracies in IOP measurements related to thinning central corneal thickness and other biomechanical changes present in these patients. The different IOP measurement methods in KC are not interchangeable. Therefore, in KC we must always monitor IOP using the same device during follow-up. Furthermore, it is necessary to carefully study possible structural and functional changes that may occur in suspected cases of glaucoma.

● **KEYWORDS:** intraocular pressure; keratoconus; tonometer; Goldmann applanation tonometry; corneal biomechanics; corneal thickness

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INTRODUCTION

The accurate measurement of intraocular pressure (IOP) is a cornerstone of the diagnosis and management of glaucoma[1-2]. Measuring IOP in patients with corneal abnormalities is challenging due to interference from various confounding factors in different measurement techniques[3-5]. In clinical practice, Goldmann applanation tonometry (GAT) is considered the gold standard method for measuring IOP, however, in patients with corneal ectasia, the measurements obtained may not correspond to reality[6-9]. Different corneal abnormalities, such as change in thickness, viscoelasticity, stiffness and curvature, motivated the development of new methods for measuring IOP[10-12].

Keratoconus (KC) is an ectatic corneal disease, which evolves with progressive non-inflammatory thinning, conical anterior projection, and is characterized by irregular astigmatism, and alteration of corneal biomechanics[13-14]. Consequently, measuring IOP in patients with KC is a major challenge due to the influence of various geometric and biomechanical factors in the readings[15-18]. Furthermore, the progression of KC can result in significant corneal changes, resulting in more errors in IOP measurements[19]. In response to IOP elevation, some KC corneas showed abnormal distensibility with significant changes in steepest point curvature. However, until now, there is no evidence that elevation of IOP can induce KC development and/or progression[20].

In eyes with KC, low ocular rigidity or a thin cornea led to falsely lower IOP measurements by GAT[8]. In simulations based on a biomechanical model of the cornea, it was demonstrated that differences in corneal biomechanics across individuals may have greater impact on IOP measurement errors than corneal thickness or curvature[16]. After assessing aqueous humor dynamics with fluorophotometry, it was noticed that KC eyes have higher outflow facilities compared to normal. Probably, the underlying biochemical defect in KC may also affect the aqueous outflow pathways[21].

High IOP is more common in adults, while KC is more common in adolescents. The prevalence of KC in United States is most common in patients aged 18 to 39y, followed by patients aged 40 to 64y[22]. Therefore, it is not only adolescents who have KC. In 2022, an estimated 4.22 million people in the United States were living with glaucoma, with a prevalence of 1.62% among people 18y or older and 2.56% among people 40y or older. Thus, it is important to screen for glaucoma at all ages[23]. Finaly, it is known that existing treatments such as scleral lenses, intracorneal ring segments, corneal collagen cross-linking (CXL) and deep anterior lamellar keratoplasty can improve but not eliminate the disease[13]. Then, patients with KC will likely live with several features of the disease, *e.g.*, irregular cornea, thin cornea, changed biomechanics, among others, for the rest of their lives. So, we have the challenge of evaluating IOP in patients with KC regardless of age group.

Challenging cases of glaucoma and KC have already been described. Reports of patients with bilateral primary juvenile open angle glaucoma[24], pseudoexfoliation glaucoma[25], steroid-induced ocular hypertension[26], steroid misuse in vernal keratoconjunctivitis resulting in steroid induced glaucoma[27], iridocorneal endothelial syndrome[28], normal-tension glaucoma[15], and KC demonstrated the need to try to improve the accuracy of IOP measurement methods in patients with KC.

To date, there are no manometric studies that demonstrate the real measurement of IOP in KC. There are many doubts regarding the best method to measure IOP in patients with KC. The present review aims to analyze existing studies on different methods of measuring IOP in KC eyes. And, mainly, encourage new studies for monitoring IOP in challenging situations such as corneal ectasia.

MATERIALS AND METHODS

This survey took place during and after the month of September 2024. Articles published from the 1950s to the present day were considered. A broad literature search was carried out in PubMed, SciELO, Embase, Web of Science, Cochrane Library with the following key words: “keratoconus”, “intraocular pressure”, “intraocular pressure measurements”, “corneal biomechanics”, “biomechanically corrected intraocular pressure”, “intrastromal corneal ring”, “tonometry”, “Pascal dynamic contour tonometer”, “ocular response analyzer”, “tonopen”, “Goldmann applanation tonometer”, “rebound tonometer”, “noncontact air tonometry”, and “Corvis ST”. The inclusion criteria adopted was the selection of articles which the main objective was to evaluate the measurement of IOP in patients with KC, regardless of the method used. Studies that measured KC characteristics such as central corneal thickness, corneal curvature, and biomechanical parameters, but did not measure IOP, were excluded. Furthermore, studies that analyzed characteristics of eyes with KC but did not have a methodological description or a detailed statistical analysis of the IOP measurement were also excluded. Two hundred and twenty-five articles were identified and their references were scrutinized, and 17 relevant to the subject matter were selected (Figure 1).

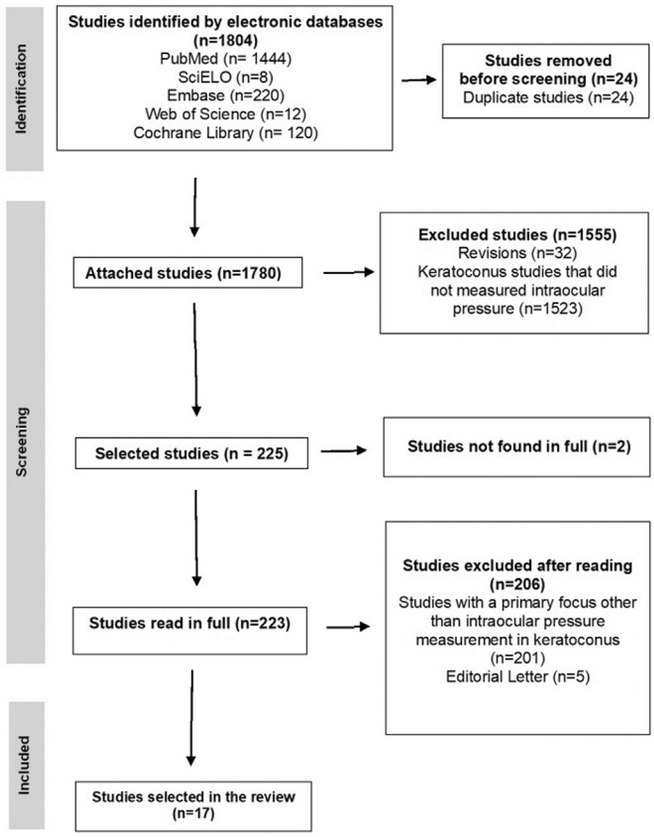

Figure 1 Study flowchart.

RESULTS

GAT in KC The everyday practice gold standard method for monitoring IOP is applanation tonometry, originally introduced by Goldmann and Schmidt in 1957[29]. And they chose a glass cone with a tip diameter of 3.06 mm for applanation of the central cornea and assumed that the Imbert-Fick law was applicable to the eye. This law determines that the internal pressure of the fluid acting on a thin layer spherical membrane is equal to the pressure which is necessary to flatten a small area of the membrane. The applicability of the Imbert-Fick law in patients with KC may not be entirely possible for some reasons: 1) The law is correct for membranes which are completely elastic and infinitely thin, and it was initially applied by Goldmann and Schmidt for corneas with medium thickness (520 to 550 μm)[29]. KC corneas are thinner than the average population, affecting the precision of tonometry measurements[30-31]. Thinner corneas such as KC generally shows falsely lower GAT results[8,32-33]; 2) The law is applied to perfectly elastic membrane spheres. However, ocular stiffness is reduced in eyes with KC compared to normal eyes, thus

altering the tonometric measurement of IOP[9,16-17]; 3) The law is valid for uniform spheres with the cornea, limbus and sclera showing homogeneous elastic properties. In normal corneas, the constitution of collagen is not uniform among the ocular structures, and it's probably more distinct in KC[34].

The IOP measurement performed by the GAT at the apex of the KC is significantly lower than measurements performed in other areas of the cornea that are less affected by the KC[35]. Furthermore, it is not only the thinning of the cornea that interferes with the measurement of IOP by the GAT, but this measurement may also be reduced in patients with large sagging cones without corneal thinning[35].

In theory, corneal curvature can interfere with GAT measurements. In more curved corneas these measurements will be artificially higher, and the opposite happens in flatter corneas. Goldmann and Schmidt recommended that for patients with a 3 D or greater astigmatism, the axis of the tonometer tip should be oriented at 43° (this angle is marked on the Goldmann tonometer prism holder with a red line) to the major axis of astigmatism (in minus cylinder). This was believed to provide the least amount of error at most corneal curvatures[36]. Although the influence of curvature occurs in the GAT measurement in normal corneas, which can lead to errors between 0.58 and 0.67 mm Hg/dioptre and in some cases up to 3 mm Hg, the correlation between corneal curvature and IOP measurement is small and not clinically relevant when considering other sources of error in measurements[37]. Despite irregular astigmatism, GAT measurements were compared in KC between with and without the astigmatism tonometer correction proposed by Goldmann and Schmidt and observed higher values were verified in the measurements performed with astigmatism correction[36]. Apart from that, it seems that GAT measurements are independent of corneal curvature in KC eyes[38-39]. Probably, other additional corneal properties of KC eyes, such as altered rigidity and elasticity, influence more GAT results.

There is a higher risk of underestimating IOP when the GAT is used at a higher altitude, particularly in eyes with glaucoma, corneal refractive surgery or thinner corneas, such as KC[40].

Due to the various uncertainties regarding IOP measurements using GAT in KC, other methods are studied and used to minimize measurement errors. We will describe below the main methods that currently exist and will table the main results of studies on these methods (Table 1)[4-5,10-12,33,36,39,41-49].

Dynamic Contour Tonometry Dynamic contour tonometry (DCT) was developed based on the Pascal law in an attempt to measure IOP independently from central cornea thickness (CCT) and other cornea properties[40]. DCT uses an applanating probe that nearly matches the corneal surface contour with a piezoelectrical device for pressure measurement attached to its apex and provides a direct and continuous transcorneal measurement of IOP with no need to apply additional forces that could modify the corneal profile. When the tip of the DCT tonometer touches the cornea, an audible signal, which changes tone with detected pressure variations, indicates correct positioning. The tip generates an electrical signal, proportional to the IOP measurement, which is automatically calculated and displayed on the digital screen along with the amplitude of the ocular pulse and the quality of each reading with a scale classified from Q1 (optimal) to Q5 (unacceptable)[50]. Clinical studies published of normal subjects indicate that IOP measurements obtained with the DCT are relatively unaffected by corneal properties[42,51-53]. Therefore, it is expected that DCT will provide a more accurate measurement of IOP in patients with KC. DCT presents higher IOP readings than GAT in KC eyes[4-5,38-39,42,53]. However, DCT may be influenced to some degree by the biomechanical properties of the cornea in eyes with irregular corneas[4,38].

TonoPen The tonoPen (TP) is a portable hand-held applanation instrument easy to carry and use. It is based on the Mackay-Marg principle and utilizes micro strain-gauge technology[54]. A 1.5 mm transducer tip, covered by a disposable single-use cap, contacts the cornea. During the straightening of the cornea by the flat base on the tip of the TP, a tightening meter creates an electrical impulse. A microprocessor senses the suitable power curves. The device then displays the average of four to ten independent readings and forms a last digital output with the percentages of variability[54]. Due to its portable nature, it is possible to use the TP to perform IOP measurements not only in the classic sitting position, but also in the supine and standing positions. It seems that higher IOP values are observed in the supine position and 5min after standing in comparison to the sitting position[55]. Another peculiar characteristic of TP is the possibility of its use for measuring IOP in diagnostic or therapeutic procedures that may involve elevation or large fluctuations in IOP, such as esophagogastroduodenoscopy[56]. When IOP measurements obtained from patients with KC are compared between TP and GAT, the results are not uniform in the literature. There are studies with higher measurements for TP[5,36,46], other for GAT[11] and another with similar results[48].

Ocular Response Analyzer The fully automated noncontact ocular response analyzer (ORA) tonometer was designed to provide IOP measurements that are independent of CCT and other corneal properties. It's an electro-optical system that uses a dynamic bidirectional applanation process in the central cornea. A precisely quantified air pulse deforms the cornea inwards, past the applanation point. After the applanation point is detected, the air is turned off and the cornea allowed to return to normal (back through the applanation point again).

Table 1 Data from studies that comparatively evaluated different IOP measurement methods in KC

Study	Type of tonometer	Number of eyes	Mean IOP (mm Hg)	*P*	Average corneal thickness (μm)	Curvature
Browning, 2004[33] (CT)	GAT	37 KC (37 patients)	10.5±2.2 (GAT)	Increase in IOP (mm Hg)/10 μm increase in CCT in KC. GAT: 0.01 (95%CI: -0.10 to 0.13; *P*=0.80); TP: -0.01 (95%CI: -0.15 to 0.12; *P*=0.84); OBF: -0.03 (95%CI: -0.20 to 0.13; *P*=0.69)	455±67 (CCT)	No information
	TP		10.9±2.7 (TP)			
	OBF		11.4±3.2 (OBF)			
Barreto *et al*, 2006[4]	GAT	10 KC, 12 control	10.3±1.8 (KC-GAT); 14.3±0.75 (control-GAT)	GAT KC *vs* control (*P*=0.024); DCT KC *vs* control (*P*=0.026)	387.8±53.3 (KC-CCT), 551±15.3 (control-CCT)	Kavg (D): 60.6±9.5 (KC), 42.7±1.7 (control)
	DCT		14.6±2.09 (KC-DCT); 17.4±3.1 (control-DCT)			
Mollan *et al*, 2008[5] (CS)	GAT	76 KC, 118 control	KC: DCT and TP>GAT (*P*<0.001), greatest concordance with GAT=IOPcc		453±55.8 (KC-CCT), 539.9±36 (control-CCT)	
	DCT					
	ORA					
	TP		Control: DCT and TP>GAT (*P*<0.001)			
Papastergiou *et al*, 2008[39] (CS)	GAT	32 KC, 46 control	10.1±1.9 (KC-GAT), 15.9±2.6 (control-GAT)	KC: GAT *vs* DCT (*P*=0.02), DCT *vs* NCT (*P*=0.02); GAT: KC *vs* control (*P*=0.002), DCT, KC *vs* control (*P*=0.03); NCT: KC *vs* control (*P*=0.003)	462±62 (KC-CCT), 544±49 (control-CCT)	Kavg (D): 47.7±3.9 (KC), 42.1±1.1 (control)
	DCT		14.85±1.5 (KC-DCT), 16.1±2.2 (control-DCT)			
	NCT (air tonometer)		9.5±2.5 (KC-NCT), 15.9±3.1 (control-NCT)			
Goldich *et al*, 2010[12] (CS)	GAT	59 KC (59 patients)	10.9±2.0 (GAT)	GAT *vs* IOPg (*P*<0.001), GAT *vs* IOPcc (*P*<0.001)	457±53.8 (CCT)	Kavg (D): 46.7±4.5
	ORA		9.5±2.8 (ORA IOPg), 13.3±2.5 (ORA IOPcc)			
Bayer *et al*, 2010[41] (CS)	GAT	120 KC (61 patients)	10.96±2.8 (GAT)	GAT *vs* IOPg (*P*<0.002), GAT *vs* IOPcc (*P*<0.0001), GAT *vs* DCT (*P*<0.0001), IOPg *vs* DCT (*P*<0.0001), IOPcc *vs* DCT (*P*<0.001)	464.08±58.4 (CCT)	No information
	ORA		10.23±3.5 (ORA IOPg), 14.65±2.8 (ORA IOPcc)			
	DCT		15.42±2.7 (DCT)			
Read and Collins, 2011[10]	DCT	20 KC, 20 control	14.3±1.4 (KC–DCT)c, 14.2±1.7 (control-DCT)c; 14.1±1.4 (KC–DCT)oc, 14.3±1.6 (control–DCT)oc	$DCT_{(AVE)}$ KC *vs* control (*P*=0.885), NCT KC *vs* control (*P*<0.0001)	493±23 (KC-CCT), 539±33 (control-CCT)	Average anterior keratometry (mm): 7.04±0.56 mm (KC), 7.83±0.23 mm (control)
	NCT (air-puff' tonometer)		9.2±1.5 (KC–NCT)c, 12.9±2.4 (control–NCT)c			
Unterlauft *et al*, 2011[42] (RCT)	GAT	114 KC (75 patients)	13.1±2.9 (GAT)	GAT *vs* DCT (*P*=0.43)	481.1±46.2 (CCT), 453.3±56.3 (MCT)	Kmax (mm): 53.8±6.5; Kmin (mm): 36.6±3.6
	DCT		14.8±2.6 (DCT)			
Gkika *et al*, 2012[43] (CS)	GAT	50 KC, 50 control	14.9±2.0 (KC–GAT), 15.8±2.0 (control–GAT)	GAT KC *vs* control (*P*=0.029); DCT KC *vs* control (*P*=0.038); ORA KC *vs* control (*P*=0.022)	449.5±38.2 (KC-CCT), 539.9±34.4 (control-CCT)	Kavg (D): 43.1±1.6 (KC), 49.2±4.2 (control)
	DCT		15.5±2.0 (KC–DCT), 16.3±1.9 (control–DCT)			
	ORA		14.1±2.4 (KC–ORA IOPcc), 15.1±2.2 (control–ORA IOPcc)			
Arribas-Pardo *et al*, 2015[44] (CS)	GAT	60 KC (60 patients)	14.3±3.6 (GAT)	GAT *vs* iCare (*P*=0.002), GAT *vs* iCare Pro (*P*=0.853)	505±53.5 (CCT)	Kavg (D): 49.2±7.5
	iCare		13.0±4.4 (iCare)			
	iCare Pro		14.2±4.1 (iCare Pro)			

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Table 1 Data from studies that comparatively evaluated different IOP measurement methods in KC (continued)

Study	Type of tonometer	Number of eyes	Mean IOP (mm Hg)	*P*	Average corneal thickness (μm)	Curvature
Altinkaynak *et al*, 2016[11] (CS)	GAT DCT TP ORA	202 KC (Amsler I-52, Amsler II-50, Amsler III-52, Amsler IV-48), 49 control	13.76±4.22 (Amsler I–GAT), 12.79±2.43 (Amsler II–GAT), 12.29±2.95 (Amsler III–GAT), 11.12±3.70 (Amsler IV–GAT), 14.19±4.90 (control–GAT), 16.66±2.91 (Amsler I–DCT), 15.97±2.57 (Amsler II–DCT), 17.03±2.85 (Amsler III–DCT), 15.94±2.65 (Amsler IV–DCT), 17.52±3.84 (control–DCT), 11.51±2.99 (Amsler I–TP), 11.09±2.47 (Amsler II–TP), 10.33±2.85 (Amsler III–TP), 9.24±2.80 (Amsler IV–TP), 13.34±4.64 (control–TP), 11.71±3.08 (Amsler I–ORA IOPg), 9.71±2.75 (Amsler II–ORA IOPg), 9.02±3.50 (Amsler III–ORA IOPg), 6.82±2.64 (Amsler IV–ORA IOPg), 13.20±5.83 (control–ORA IOPg), 13.87±2.32 (Amsler I–ORA IOPcc), 13.89±2.45 (Amsler II–ORA IOPcc), 13.73±2.36 (Amsler III–ORA IOPcc), 13.22±2.46 (Amsler IV–ORA IOPcc), 13.30±5.54 (control–ORA IOPcc)	GAT: I *vs* IV, II *vs* IV, III *vs* control, IV *vs* control (*P*<0.05); TP: I *vs* IV, II *vs* IV, II *vs* control, III *vs* control, IV *vs* control (*P*<0.05); IOPg: I *vs* II, I *vs* III, I *vs* IV, II *vs* IV, II *vs* control, II *vs* IV, III *vs* control, IV *vs* control (*P*<0.05)	KC: Amsler I 475.4±44.2, Amsler II 460.3±23.9, Amsler III 455.2±24.4, Amsler IV 426.3±51.1; control: 531.1±40.6	Mean sim K (D): KC: Amsler I 47.6±1.18, Amsler II 50.4±1.76, Amsler III 54.8±1.11, Amsler IV 57.4±3.82; control: 44.37±1.81
Özcura *et al*, 2017[45] (CS)	GAT DCT iCare	63 KC (63 patients)	11.72±2.59 (GAT) 15.42±3.31 (DCT) 9.34±3.29 (iCare)	GAT *vs* DCT (*P*<0.001), GAT *vs* iCare (*P*<0.001), DCT *vs* iCare (*P*<0.001)	423.06±59.64 (CCT)	CR (mm): 6.23±0.84
Arribas-Pardo *et al*, 2017[46] (RCT)	GAT DCT iCare TP	91 KC (91 patients)	14.1±3.41 (GAT) 15.0±3.17 (DCT) 13.4±4.09 (iCare) 14.9±3.58 (TP)	GAT *vs* DCT (*P*=0.002), GAT *vs* iCare Pro (*P*=0.021), GAT *vs* TP (*P*=0.007)	500±49.2 (CCT)	Kavg (D): 49±5.4
Mendez-Hernandez *et al*, 2017[47] (OS)	GAT DCT iCare Pro TP ORA	174 KC (174 patients/74 with ICRS)	14.5±2.8 (GAT), 14.4±3.5 (GAT-ICRS) 16.1±3.4 (DCT), 15.1±3.3 (DCT-ICRS) 14.0±3.90 (iCare Pro), 13.9±4.30 (iCare Pro-ICRS) 15.4±3.5 (TP), 15.3±3.5 (TP-ICRS) 8.9±3.8 (ORA IOPg), 8.3±3.5 (ORA IOPg-ICRS), 13.0±3.2 (ORA IOPcc), 12.3±3.3 (ORA IOPcc-ICRS)	With *vs* without ICRS: GAT (*P*=0.847), DCT (*P*=0.098), iCare Pro (*P*=0.914), TP (*P*=0.844), ORA IOPg (*P*=0.210), ORA IOPcc (*P*=0.363)	495.8±46.0 (CCT)	Kavg (D): 49.1±5.9
Merola *et al*, 2022[36]	nGAT cGAT TP	39 KC (24 patients)	11.3±2.6 (cGAT) 9.9±2.6 (nGAT) 12.3±3.1 (TP)	cGAT *vs* nGAT (*P*<0.01), cGAT *vs* TPA (*P*=0.004), nGAT *vs* TPA (*P*<0.01)	469±75.8 (CCT)	Kavg (D): 50.4±5.30
Yildiz, 2023[48]	GAT Easyton TP iCare	46 KC (26 patients)	10.67±1.52 (GAT) 12.33±1.65 (Easyton) 11.59±2.17 (TP) 10.04±2.33 (iCare)	GAT *vs* Easyton (*P*<0.001), GAT *vs* TP (*P*=0.154), GAT *vs* iCare (*P*<0.732), TP *vs* iCare (*P*=0.001), TP *vs* Easyton (*P*=0.421)	466.95±46.87 (CCT)	Kavg (D): 48.6±4.53; Kmax (D): 56.25±7.56
Scholte *et al*, 2025[49] (CS)	GAT iCare NCT	74 KC (74 patients–one eye with ICRS and the other without)	11.5±2.6 (GAT), 11.2±2.7 (GAT-ICRS) 10.4±3.4 (iCare), 9.4±3.2 (iCare-ICRS) 13.2±2.4 (NCT), 12.1±2.2 (NCT-ICRS). IOP measured 90d after ICRS implantation	With *vs* without ICRS: GAT (*P*=0.211), iCare (*P*=0.137), NCT (*P*=0.021)	No information	No information

IOP: Intraocular pressure; KC: Keratoconus; DCT: Dynamic contour tonometry; NCT: Non-contact; c: Central measurement; D: Diopter; oc: Off central measurement; AVE: Average; CCT: Central corneal thickness; RCT: Randomized controlled trial; GAT: Goldmann applanation tonometry; MCT: Minimal corneal thickness; Kmax: Maximum keratometry; Kmin: Minimum keratometry; Kavg: Average keratometry; CS: Comparative study; ORA: Ocular response analyzer; IOPcc: Corneal-compensated IOP value; CH: Corneal hysteresis; CRF: Corneal resistance factor; TP: Tonopen; IOPg: Goldmann-correlated IOP value; nGAT: No astigmatism correction Goldmann applanation tonometer; cGAT: Astigmatism corrected Goldmann applanation tonometer; Easyton: Easyton transpalpebral tonometer; CR: Mean corneal radius of curvature; OBF: OBF pneumotonometer; CT: Clinical trial; OS: Observational study; CI: Confidence interval; ICRS: Intrastromal corneal ring segments.

It provides two applanation measurements within 20ms, one when the cornea is flat on the way in and the other on the way out. Two independent pressure values are derived from these inward and outward applanation points, IOPg and IOPcc. IOPg is the average of the two applanation pressure points, the Goldmann-correlated IOP value. IOPcc is a corneal-compensated IOP value, where the difference between the two pressure readings is calculated and termed corneal hysteresis (CH), and this is then used to calculate IOPcc. The viscous damping of the cornea is the CH. The corneal resistance factor (CRF) is a measurement derived from viscous and elastic resistance to the air pulse[18,41,57]. CH is used as a parameter to characterize the biomechanical status of the cornea, and it's lower in KC than in normal eyes[18], and in KC with glaucoma than KC without glaucoma[15]. In comparison to GAT IOP values in KC eyes, IOPg presents lower and IOPcc higher measurements[5,11-12,17,41]. Furthermore, IOPcc was found to be independent of CCT[41]. In another study, unlike GAT measurements, ORA readings seemed to be affected mainly by corneal curvature[12].

Corneal Visualization Scheimpflug Technology The corneal visualization scheimpflug technology (Corvis-ST) is a relatively new noncontact tonometer that analyses the corneal biomechanical properties[58-59]. It emits a pulse of air, which applanates and indents the cornea. It differs from the ORA because it uses an ultra-high speed Scheimpflug camera (4330 frames/s) to record *in vivo* cross-sectional images of the cornea during and after application of the air pulse. There are limited studies about the repeatability of the IOP, CCT, and deformation amplitude in normal and KC eyes[60]. The new Corvis-ST Software provides parameters such as the maximum value of the ratio between deformation amplitude at the apex 1 mm and 2 mm from central cornea [DA Ratio Max (1 mm), DA Ratio Max (2 mm)], biomechanical corrected IOP (bIOP), Ambrósio's relational thickness horizontal, stiffness parameter at first applanation, corvis biomechanical index[61-62]. Recent study found that these new parameters had detectability for distinguishing KC eyes from normal eyes[62]. It was demonstrated that Corvis-ST parameters are highly repeatable in KC[53,63], and deformation amplitude is significantly greater in KC than healthy eyes, even when controlled for IOP[63]. bIOP was clinically validated in patients with KC and soft corneas and this method to estimate IOP significantly reduced the dependence on corneal biomechanics[64].

Rebound Tonometer Rebound tonometer (RBT) is a handheld, lightweight, and contact tonometer that use the impact rebound principle to measure IOP[65]. It consists of 2 coaxial coils that impel a magnetized probe toward the cornea and records IOP by detecting the deceleration of a rod probe as it is bounced off the cornea. This movement is detected by a solenoid inside the instrument. Similarly to TP, it is also possible to perform IOP measurements with the RBT not only in the classic sitting position, but also in the supine and standing positions, thus allowing a more comprehensive assessment of IOP in specific cases[55]. The RBT can determine IOP in pathologic cornea and post-keratoplasty[66]. However, the agreement between GAT and RBT was clinically acceptable in corneal dystrophy, KC, and lamellar keratoplasty but poor in eyes after penetrating keratoplasty or in those with corneal edema[67-68]. RBT readings are, generally, on average, similar to GAT readings in normal eyes[69], however, in KC eyes it alternates between higher[17] and lower measurements[45]. When assessing the two models of RBT, icare and icare Pro, it was showed similar GAT IOP values with iCare Pro and lower values with iCare in KC[44].

Non-Contact Tonometer Non-contact tonometer (NCT) applanates the cornea by a jet of air, so there is no direct contact between the device and the surface of the eye. The force of the air jet increases rapidly and linearly with time. The instrument also emits a collimated beam of light that is reflected from the central cornea and then received by a photocell. When an area of the cornea 3.6 mm in diameter is flattened, the light reflected to the photocell is at a maximum. The time required to produce the peak reflection is directly related to the force of the air jet and thus to the counterbalancing IOP[54]. Similarly to GAT, NCT IOP measurements are more dependent on corneal abnormalities such as irregular corneal curvature and thinned cornea than DCT in KC eyes[10].

DISCUSSION

Summary of the Advantages and Limitations of the all Mentioned IOP Measuring Approaches in KC Eyes Although GAT is the gold standard for measuring IOP, in eyes with KC lower measurements are observed due to the thin cornea and other biomechanical features[8,32-33,36,38]. Generally, DCT in KC has higher IOP readings than GAT[4-5,38-39,42,53]. Although DCT IOP measurements are relatively unaffected by corneal properties[42,51-53], it may be influenced to some degree by the biomechanical properties of the cornea in eyes with irregular corneas[4,56]. TP shows higher[5,36,46], lower[11] and similar[48] IOP measurements in comparison to GAT in KC eyes. One TP advantage is that it is possible to perform IOP measurements not only in the classic sitting position, but also in the supine and standing positions. In comparison to GAT IOP values in KC eyes, ORA IOPg presents lower and ORA IOPcc higher measurements[5,11-12,17,41]. Additionally, IOPcc was found to be independent of CCT[41]. However, ORA readings seemed to be affected mainly by corneal curvature[12]. Corvis-ST bIOP was clinically validated in patients with KC and soft corneas and this method to estimate IOP significantly reduced the dependence on corneal biomechanics[64]. Corvis-

ST parameters are highly repeatable in KC[58,63]. The agreement between GAT and RBT was clinically acceptable in KC[67-68]. RBT readings are, generally, on average, higher than GAT readings in normal eyes[69], however, in KC eyes it alternates between higher[17] and lower measurements[45]. When assessing the two models of RBT, iCare, and iCare Pro, it was showed similar GAT IOP values with iCare Pro and lower values with iCare in KC[44]. Similarly to TP, RBT can be used in different positions, such as classic sitting, supine and standing[55]. Similarly to GAT, NCT IOP measurements are more dependent on corneal abnormalities such as irregular corneal curvature and thinned cornea than DCT in KC eyes[10].

Limitations of the Studies Analyzed Some studies analyzed in the Present research included one eye of some KC patients and also both eyes of other KC patients. This situation may constitute a limitation of the results of some these studies owing to the fact that when both eyes of the same patient are included, specific statistical methods must be applied, such as Bootstrap or generalized estimating equations. Although KC patients may have their own eyes at different stages of the disease, when both eyes of the same patient are in the same group and inter-eye correlation is ignored, *P*-values may be lower than they should be without adequate statistical treatment.

IOP Measurement After Corneal Collagen Cross-Linking CXL is a surgical treatment used to strengthen the corneal tissue in KC with riboflavin and ultraviolet A[70]. Riboflavin acts as a photosensitizer that is activated by ultraviolet A light and oxygen radicals' production leads to the development of covalent bonds between collagen fibrils, increasing biomechanical corneal stiffness. After CXL with riboflavin and ultraviolet A for KC, an increase in IOP measured by GAT, ORA, and DCT was detected in one study with[70] and in others without[43,71] statistical significance. The increase is probably the result of an increase in corneal rigidity.

IOP Measurement After Corneal Ring Segments Intrastromal corneal ring segments (ICRS) are used to delay or stop disease progression of KC, and usually avoid or delay the need for penetrating keratoplasty[44,46]. ICRS flatten and strengthen the cornea and thus reduce asymmetrical astigmatism, improving visual acuity in most cases[44,46]. Changes in corneal biomechanics caused by the presence of ICRS in the corneal stroma could affect the capacity of GAT to accurately measure IOP. Neither cornea astigmatism, cornea curvature, nor the number of ICRS seems to influence IOP values either in GAT or in RBT in eyes with KC with ICRS [44]. And, in these patients, GAT and iCare Pro showed similar IOP values[44]. In KC eyes fitted with ICRS, IOP readings obtained with iCare Pro and TP showed most agreement with GAT, and DCT slightly overestimate GAT measurements[46]. When comparing IOP measurements among GAT, iCare Pro, DCT, TP and ORA in KC eyes with and without ICRS no difference was found[47]. Also no clinical significative difference was found between KC eyes with and without ICRS when comparing GAT, iCare, and NCT measurements[49].

IOP in Daily Curve of Intraocular Pressure It is widely known that IOP varies throughout the 24h of the day. Daily curve of IOP based on IOP values acquired by applanation tonometry at 6:00 *a.m.*, in dark, with the patient lying down in bed, is extremely important in establishing the diagnosis of glaucoma suspect and assessing IOP in glaucoma[72]. It has been shown that IOP increases in the supine position and this may explain why some patients with glaucoma show progression in an apparently normal tension or in compensated situation[36]. In one study, the IOP of 73 KC eyes was assessed using a pneumotonometer from 7:00 *a.m.* to 10:00 *p.m.,* and it was found the mean upper value of 19.24±2.84 mm Hg for right eye and 18.06±2.80 mm Hg for left eye[73]. In another study, IOP was measured from 6:00 *a.m.* to 10:00 *p.m.* using GAT and TP in 39 KC eyes[36]. And the measurement at 6:00 *a.m.* was performed in the dark, with the patient lying down in bed[36]. IOP peaks of daily curve were identified at 6:00 *a.m.*, and TP mean values (12.3±3.1 mm Hg) were higher than GAT with (11.3±2.6 mm Hg) and without (9.9±2.6 mm Hg) the correction of the astigmatism values[36].

This study aimed to conduct an extensive and thorough review of the topic of KC and IOP measurement. The vast majority of studies were based on the comparison of different methods of measuring IOP. Thus, we found a lack of prospective studies and also of basic sciences on the topic. Some recent studies used combination of clinical data, multimodal imaging[74], and artificial intelligence[75], and included IOP as one of the clinical parameters evaluated for the early diagnosis of KC and its biomechanical assessment. However, they did not study the accuracy of IOP measurement. We hope that this review will serve as an incentive for researchers to delve deeper into a topic that still requires many answers.

CONCLUSION

As far as we know, there are no manometric studies in patients with KC. Therefore, we don't know the real behavior of IOP in these cases. Considering the available knowledge, IOP measurements taken with GAT probably underestimate the real values in patients with KC. Possibly, IOPcc, DCT, bIOP can reduce some inaccuracies in IOP measurements related to CCT and biomechanical changes present in KC. However, till now, they cannot be considered the gold standard for measuring IOP in these patients because they may also be affected by KC severity. So, it is extremely important to evaluate structural and functional changes when analyzing patients with KC and ocular hypertension, or suspected glaucoma, or glaucoma. And,

when we assess IOP, measurements from different devices are not interchangeable. Therefore, in KC we must always monitor IOP using the same device during the follow up. Whenever possible, we should use more than one IOP measurement method. We believe that the evaluation of the accuracy of IOP measurement methods in patients with KC still represents a gap to be filled by new studies.

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