Normative Quantitative Values for Dacryoscintigraphy and the Effect of Lid Massage

Brad Guo[1], Chong Ghee Chew[2], Valerie Juniat[3], Dinesh Selva[3], and Mikayla Dimitri[2]

[1]Department of Ophthalmology, Sydney Eye Hospital, Sydney, NSW, Australia; [2]Department of Nuclear Medicine, PET, and Bone Mineral Densitometry, Royal Adelaide Hospital, Adelaide, South Australia, Australia; and [3]Department of Ophthalmology, Royal Adelaide Hospital, Adelaide, South Australia, Australia

Our objectives were to establish normative quantitative values for dacryoscintigraphy in an older population and to evaluate the effect of lid massage. **Methods:** We conducted a prospective study of 44 eyes of 22 participants aged between 54–90 y that had no symptoms of epiphora and no clinical tear film instability, lid abnormality, lacrimal system impairment, or patent lacrimal duct on syringing. Dacryoscintigraphy was performed and interpreted by a single nuclear medicine physician. The scan protocol involved instillation of ^{99m}Tc-pertechnetate in each eye, with a 45-min scan performed with 1-min frames. Lid massage and a sinus clearing maneuver were then performed, followed by a further 45 min of scanning. **Results:** The mean age of the 22 participants was 71.9 y. Quantitative analysis by half-clearance time (HCT) demonstrated a median presac HCT of 25.5 ± 15.0 min and a whole-eye HCT of 40.0 ± 19.5 min. There was no association between age or sex and HCT. Qualitatively, 29 of 44 eyes (66%) appeared to have at least 1 region of delayed clearance, with improvement noted in 23 after lid massage (79%). **Conclusion:** We report the quantitative values for dacryoscintigraphy in an asymptomatic older population who had normal findings on lacrimal examination. A high rate of delay in radiotracer transit on qualitative examination suggesting a low specificity. The false-positive rate was significantly improved with the novel approach of adding lid massage, and the significance of this finding merits further research.

Key Words: dacryoscintigraphy; lacrimal; normative; quantitative

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Epiphora is a common ophthalmic condition encountered in the eye outpatient clinic. The workup involves differentiating hypersecretion from an anatomic or functional failure in the drainage of tears. When anatomic causes of epiphora are excluded, ophthalmologists may evaluate patients for a functional delay in tear drainage, which can be assessed with dacryoscintigraphy.

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For correspondence or reprints, contact Chong Ghee Chew (ghee.chew@sa.gov.au).
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Dacryoscintigraphy as a nuclear scan for the evaluation of epiphora was first reported in 1972 (*1*). Compared with dacryocystography, dacryoscintigraphy offers a superior physiologic assessment of lacrimal flow (*2*). It is considered a useful investigation that can detect abnormalities in 80%–95% of symptomatic patients who had previously demonstrated a patent lacrimal system on syringing (*3,4*). Dacryoscintigraphy has good clinical applicability because of its sensitivity and noninvasive technique (*3*).

It has been our observation that massaging the lid during the course of dacryoscintigraphy appears to facilitate transit of radiotracer from the conjunctival sac to the nasal cavity. The exact mechanism for this observation is unclear. It may relate to the facilitation of movement of tears into the nasolacrimal sac, which is an active process brought on by the combined action of the lid and orbital components of the orbicularis oculi muscle during the act of blinking, a mechanism referred to as the lacrimal pump.

In this paper, we report the normative values of dacryoscintigraphy in an asymptomatic, older Australian population using a robust methodology that recruited asymptomatic patients in an appropriate age group while clinically excluding other factors that may lead to delayed tear drainage. As part of the study, we also evaluated the effect of lid massage on radiotracer transit.

MATERIALS AND METHODS

Subjects

This was a prospective, cross-sectional survey of participants presenting to the ophthalmology clinic at the Royal Adelaide Hospital. We screened for participants who had a presenting complaint unrelated to the anterior segment or lid pathology (e.g., reviewed for retinal pathology). The study was performed between April 2018 and February 2021, was approved by Royal Adelaide Hospital Ethics Committee (reference number R20171130 HREC/17/RAH/532), and adhered to the tenets of the Declaration of Helsinki. Informed written consent for the study was obtained from all participants.

Inclusion Criteria

Participants aged between 40–90 y were recruited. Only patients who reported no symptoms of unilateral or bilateral epiphora were considered.

Exclusion Criteria

Patients with a reported history of hypersecretion etiologies, severe dry eye, blepharitis, orbicularis dysfunction (cranial nerve pathology), lid position abnormality (significant lid laxity, entropion, ectropion), punctal abnormality (congenital or acquired), and pregnancy were excluded.

Clinical Assessment

Patients were examined clinically for tear meniscus height, sufficient tear production (Schirmer test), tear break-up time, lid laxity (snap-back test, distraction test, medical canthal tendon laxity, lateral canthal tendon laxity), evidence of lid disease (e.g., conjunctivochalasis or mucocele), or reflux from lacrimal syringing. Patients who demonstrated abnormalities on examination were excluded from the study.

Dacryoscintigraphy Technique

Dacryoscintigraphy was performed in accordance with the standard technique at Royal Adelaide Hospital. Ten microliters (3 MBq) of ^{99m}Tc-pertechnetate were dispensed topically (using a 10-μL pipette holder) onto the participant's conjunctival sac in both eyes while the participant was lying supine. The participant then sat erect, with head and chest straps applied, looking straight at the γ-camera (Intevo 16 [Siemens Healthineers], 128 × 128 matrix, pinhole collimator) while blinking normally. One-minute sequential images were taken with the γ-camera over 45 min. At the end of serial scanning, the participant was asked to clear the nasal passages by blowing the nose, and a single scan was performed subsequently. Gentle circular massage was applied over each lid with the participant's eyes closed. Another 45 min of 1-min sequential scanning was subsequently performed.

Quantification Method

Decay-corrected radioactivity counts were determined for 2 separate regions of interest (ROIs): presac (right eye, ROI 1; left eye, ROI 3) and postsac (right eye, ROI 2; left eye, ROI 4) as shown in Figure 1. The activity in each ROI was also corrected for background activity determined in a triangular ROI between the presac and postsac ROIs. Scans at 5-min intervals were chosen to quantify activity in the ROIs. Images with motion artifacts were not used; rather, an earlier or later image without patient movement was used. We pooled the data for ROIs 1 and 3 as the presac region. We summed ROIs 1 and 2 as the whole-eye region for the right eye, and we summed ROIs 3 and 4 as the whole-eye region for the left eye. We then pooled the summed data as a collective whole-eye region dataset.

The decay-corrected radioactivity for the presac region and the whole-eye region for each participant was then plotted against time (Fig. 2). A linear line of best fit was applied, and the half-clearance time (HCT) was calculated for each region for up to 30 min. The study protocol was for 45 min of scanning, which most participants found to be too long to tolerate. One participant was inadvertently scanned for only 30 min. For this combination of reasons, we chose to generate HCTs for a 30-min acquisition, which is also our standard clinical protocol for this test.

Measured Outcomes

Primary Endpoint. The primary endpoint was quantitative assessment of the lacrimal system, measuring the HCT of the presac and the whole eye. The presac region was defined as the conjunctival sac and the lacrimal canaliculi (ROIs 1 and 3). The whole eye was defined as the presac region plus the postsac region, defined as the nasolacrimal sac and nasolacrimal duct (ROIs 1 + 2 and 3 + 4). The HCTs of the presac and whole-eye regions were determined for the pre– or non–lid massage (NLM) dataset and the post–lid massage (PLM) dataset.

Secondary Endpoint. The secondary endpoint was qualitative assessment of the lacrimal system, focusing on the proportion of

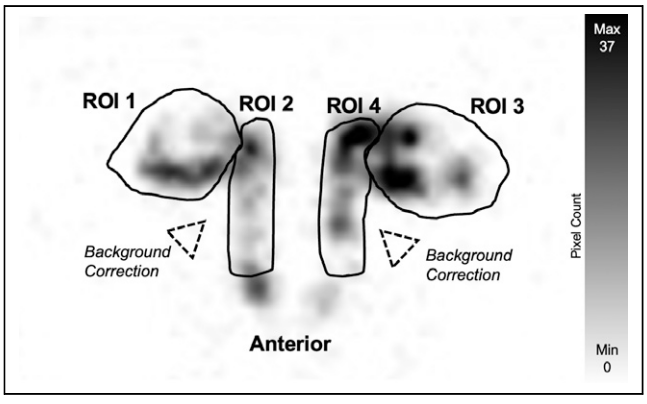

FIGURE 1. Example of presac ROI (ROI 1, right eye; ROI 3, left eye) and postsac ROI (ROI 2, right eye; ROI 4, left eye) used in this study. Background correction was subtracted in final quantitative analysis.

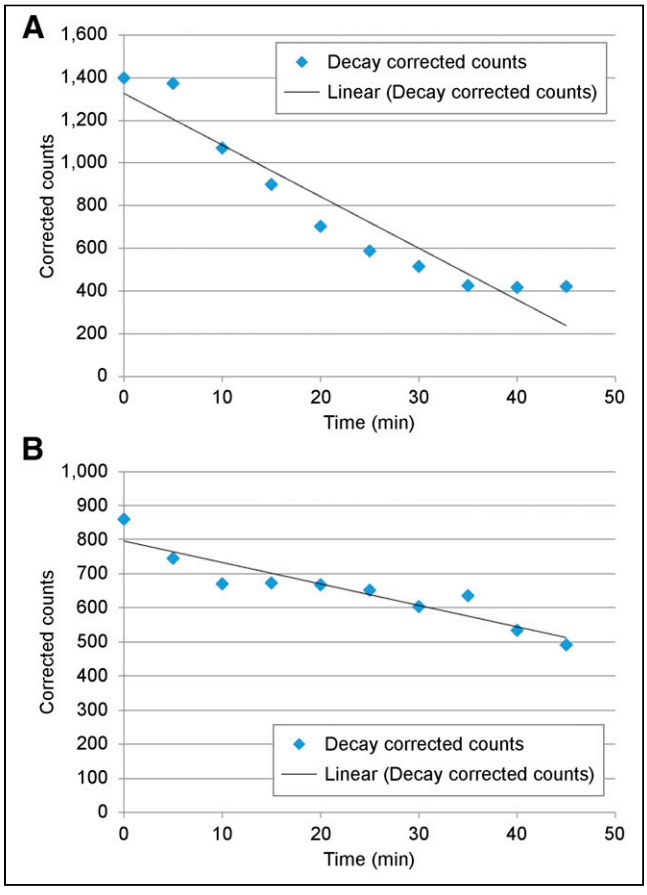

FIGURE 2. Example of ROI decay-corrected counts presented as scatterplot. (A) Time–activity curve of study with normal clearance on qualitative assessment. (B) Time–activity curve of study with scan appearance of delayed radiotracer clearance.

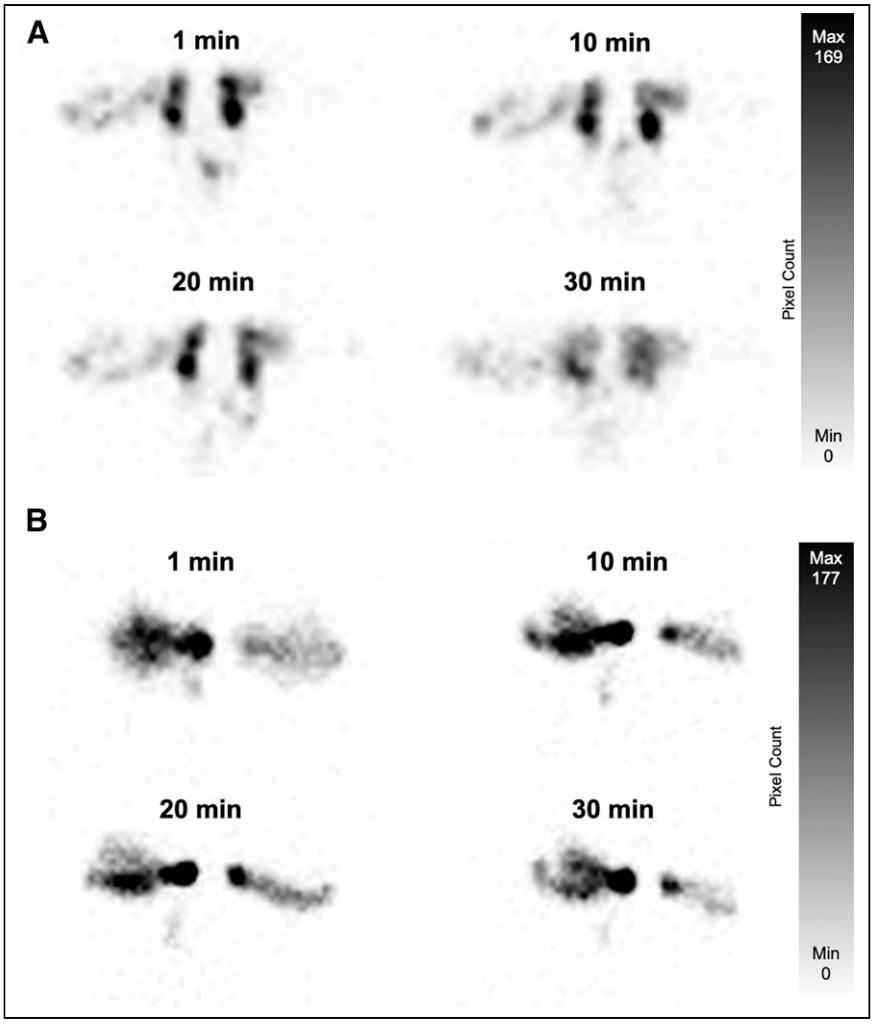

FIGURE 3. (A) Example of dacryoscintigraphy study in our series that demonstrates normal lacrimal system with no regional delay in radiotracer transit. (B) Study that demonstrates bilateral postsac delay. This was interpreted as false-positive study because the participant did not have symptoms of epiphora and had no clinical signs to explain lacrimal system pathology.

normal scans, defined as scans showing uninterrupted transit from the presac to the postsac regions and transit from the postsac region with visualization of activity in the nose (Fig. 3). Also assessed was improvement of radioactive tracer movement for PLM (Fig. 4).

Statistical Analysis

Statistical analyses were performed with Jamovi, version 1.6 (https://www.jamovi.org).

We found that the distribution of HCTs in our study were right-skewed; therefore, our HCT results are presented as medians with interquartile ranges.

Linear regression modeling was performed to assess the relationship between HCT and age. Both correlation coefficient (R^2) and BG check are presented. A Mann–Whitney U test was performed to determine the relationship between sex and HCT, with P values being 2-sided and considered statistically significant when values were less than 0.05.

RESULTS

Forty-four eyes were analyzed from 22 participants. One participant declined the postmassage study. His premassage data were included in the analyses. Thus, 172 data points were acquired, 168 (98%) of which were used. Three of the 4 excluded data points were because no net clearance had been recorded (1 whole-eye region before massage, 2 presac regions after massage). The fourth excluded datum was of a whole-eye region before massage that had an HCT of 485 min and was considered an outlier that was skewing the results.

Demographics

The mean age of the participants was 71.9 y (SD, 9.8 y), with a range of 54–90 y. There were 14 (63.6%) male participants (Table 1).

Quantitative Results

HCT results did not significantly differ between the 2 eyes of the participants (Table 2).

The median HCT for the presac region was 25.5 min (range, 17–112 min; interquartile range, 15.0 min) with NLM and 71.0 min (range, 41–287 min; interquartile range, 35.5 min) with PLM (Table 3). There was a statistically significant difference between the HCT times for presac clearance NLM compared with PLM ($P < 0.001$).

The median HCT of the whole eye was 40.0 min (range, 18–193 min; interquartile range, 19.5 min) with NLM and 55.5 min (range, 20–225 min; interquartile range, 33.0 min) with PLM. There was no statistically significant difference in the HCT of the whole eye between NLM and PLM ($P = 0.12$).

We analyzed for a correlation between age and HCT with linear regression modeling (Table 4). The R^2 value was low, and the P value was not statistically significant for HCT regardless of presac or whole eye and NLM or PLM status. A Mann–Whitney U test for sex was performed, which once again showed no statistically significant difference between sex and HCT.

Qualitative Outcomes

Our nuclear physician coinvestigator reviewed all images qualitatively. In 29 of 44 eyes (66%) of 15 participants for NLM, at least 1 abnormal ROI was demonstrated, which we defined as delayed movement of radioactive tracer from either the presac or the postsac regions. Of these 29 eyes,

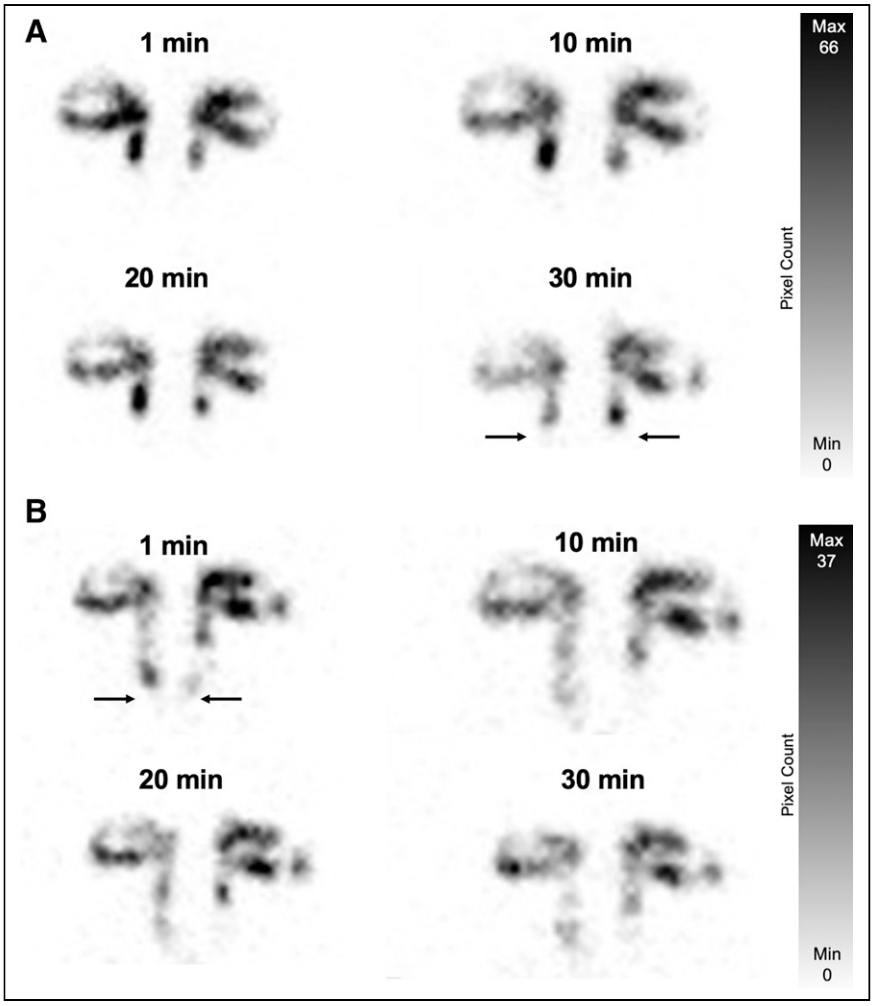

FIGURE 4. (A) Example of dacryoscintigraphy study in our series that initially demonstrated no nasal radioactivity (arrow) bilaterally. (B) In the same participant, flow of radioactivity into nasal cavity after lid massage. We interpreted this as false-positive study that was averted with lid massage.

abnormal radiotracer transit was noted in 6 presac and 23 postsac regions.

For PLM, 23 of 29 eyes (79%) in 13 participants improved and demonstrated normal-appearing radioactive tracer movement, defined as visible progress of radioactivity transit (Fig. 4). Improvement was demonstrated in 2 of 6 eyes (33%) with abnormal presac regions and 19 of 23 eyes (83%) with abnormal postsac regions.

The nose-blowing maneuver preceded the lid massage. Of those with improvement, in only 1 participant was there an improvement in the postsac region of both eyes after blowing her nose. Thus, the predominant benefit to test specificity was from the lid massage maneuver.

DISCUSSION

We report the normative quantitative values and qualitative evaluation of dacryoscintigraphy in asymptomatic individuals using a robust methodology to exclude those likely to present lacrimal drainage pathology. We chose HCTs for our quantitative analyses. We evaluated the effect of lid massage on the study outcomes.

NLM

Quantitative Assessment. For the NLM dataset, the quantitative analysis by HCT demonstrated a median presac HCT of 25.5 ± 15.0 and a whole-eye HCT of 40.0 ± 19.5.

Quantitative references values will be valuable in enhancing the ability of dacryoscintigraphy to guide epiphora diagnosis and management. Interobserver agreement for dacryoscintigraphy findings ($\kappa = 0.36$) has been reported to be lower than that for dacryocystography ($\kappa = 0.55$) (*5*). For this reason, robust baseline values that are applicable to the older demographic of patients who would present for workup of epiphora are needed to improve clinical confidence in this investigation.

When compared with transit time, we believe HCT to be a preferrable method of quantitative dacryoscintigraphy interpretation as it is intuitive and easy to generate. Studies described by Chavis (*6*) and Carlton et al. (*7*), evaluating transit time to structures, may have limitations due to variability in the time between radiotracer administration (applied with

TABLE 1
Participant Characteristics

Characteristic	Data
Eyes (*n*)	44
Age (y)	
Mean	71.9 (SD, 9.8)
Range	54–90
Male (*n*)	14 (63.6%)

TABLE 2
Comparison of Difference Between Both Eyes of Participants

Parameter	Mean difference (min)	*P*
HCT presac NLM	8.14	0.13
HCT whole-eye NLM	2.20	0.85
HCT presac PLM	6.76	0.49
HCT whole-eye PLM	1.25	0.85

TABLE 3
Median HCT for Lacrimal Structures

Parameter	NLM (min)	PLM (min)	*P*
HCT presac			<0.001
Median	25.5	71.0	
Interquartile range	15.0	35.5	
Range	17–112	41–287	
HCT whole eye			0.12
Median	40.0	55.5	
Interquartile range	19.5	33.0	
Range	18–193	20–225	

the participant supine in our study) and positioning of the patient erect in front of the pinhole collimator, particularly in patients with limited mobility.

Our quantitative analyses involved radiotracer clearance of the presac region (defined as the conjunctival sac and the lacrimal canaliculi) and the whole-eye region (defined as the presac region and the postsac region, the latter consisting of the nasolacrimal sac and the nasolacrimal duct). We did not analyze postsac structures separately, as the clearance of this region is totally dependent on the clearance of the presac region. HCT is a measure of the rate of clearance of 50% of radioactivity from an ROI after a known and fixed amount of radiotracer has been administered. As a quantitative parameter, its validity is compromised or invalidated if there is an ongoing delayed delivery of radioactivity into the ROI. For the postsac region, there is an ongoing feeding of radioactivity at variable and uncontrolled rates from the presac region. Thus, a whole-eye HCT was used instead of a postsac HCT. If used in a clinical study of a patient with epiphora, a presac obstruction could potentially result in a falsely delayed postsac HCT because of the ongoing filling by the presac structures. We rationalized that a presac obstruction would likely demonstrate a prolonged presac HCT and probably whole-eye HCT. A postsac obstruction would likely demonstrate a prolonged whole-eye HCT.

To the best of our knowledge, published normative studies to date are limited in clinical application as they have studied lacrimal systems in low participant numbers, recruited a young age group of between 23.5 and 40 y, based assessment of normal on symptoms alone, or defined normal as the asymptomatic eye in unilateral epiphora (*6–11*). Previous studies do not reflect the average 60- to 70-y age of patients presenting with epiphora (*3*). Patients who have abnormalities in their symptomatic side of the lacrimal drainage apparatus may also have subclinical obstruction in their asymptomatic side, leading to inaccurate normal dacryoscintigraphy values (*12*). Hence, the specificity of dacryoscintigraphy remains unclear.

TABLE 4
Relationship of HCT with Age and Sex

		P	
Parameter	Age (R^2)	Age	Sex
HCT presac NLM	0.01	0.48	0.53
HCT whole-eye NLM	0.02	0.40	0.29
HCT presac PLM	0.08	0.08	0.62
HCT whole-eye PLM	0.01	0.61	0.22

Using the quantitative method of HCT, our results are significantly higher than those of Hurwitz et al. (*8*), who reported a 4.1-min HCT at the palpebral aperture (equivalent to our presac region) and 5.2 min at the nasolacrimal duct in erect patients. In supine patients with closed eyes, there is a reported mean HCT of 38.0 min at the palpebral aperture and 18.0 min at the nasolacrimal duct. There is a key difference in the methodology described, as the study of Hurwitz et al. used a different radiotracer, ^{99m}Tc-sulfur colloid. Our institution uses ^{99m}Tc-pertechnetate as part of a well-established protocol in an old test. The advantages of ^{99m}Tc-pertechnetate are its availability and ease of preparation, and the potential disadvantage is conjunctival mucosal absorption, which may contribute to radiotracer clearance. Our study is the only normative study to report quantitative values for ^{99m}Tc-pertechnetate. Despite the use of sulfur colloid, the HCTs of the study of Hurwitz et al. were unexpectedly shorter than ours for an unclear reason. The population of their study was significantly younger (25–40 y), although we did not find a correlation with age and HCT results in our study. Finally, their normative study evaluated only 14 eyes.

In the study of Doucet et al. (*9*), once again utilizing sulfur colloid as the radioactive tracer, the mean HCT at the palpebral aperture was 3.5 min. There was no reported mean age for participants in this study, and the study duration was limited to 12 min. Patients were syringed immediately before administration of the dacryoscintigraphy; therefore, manipulation of the nasolacrimal system may interfere with interpretation of supposedly normative dacryoscintigraphy results. We performed lacrimal syringing days to weeks before the participants underwent dacryoscintigraphy imaging and therefore believe our protocol would be consistent with typical clinical practice.

In this study, we included background correction for completion. In retrospect, the background activity was noted to be so low as not to affect the analyses and could be discarded if our technique were to be used in clinical practice.

With regard to study duration, 45 min of imaging was not tolerated well by some participants, resulting in head movement despite the head strap. Therefore, quantitative analysis up to a 30-min acquisition is a more suitable protocol in practice and is likely to result in fewer motion artifacts. A 30-min study is also the standard clinical protocol for our institution. Patient movement is a major confounding factor in quantification if the study is analyzed as a continuous dataset. To circumvent this factor, we chose from the 1-min data at 5-min intervals for quantification. If movement was noted at a preset interval, the image before or after was used instead.

We recruited an older patient demographic than in previous studies, aiming to reflect populations more likely to present with epiphora. We did not find a statistically significant association with age and HCT. We acknowledge the small number of participants. Future studies using a similar technique and higher recruited numbers may be able to demonstrate differences between younger and older patients. There is some evidence in the literature in the form of clinical tests such as the Jones test that lacrimal transit time through the nasolacrimal duct may become slower with increasing age, and the drainage capacity to the nose also decreases (*13,14*).

Qualitative Assessment. Qualitatively, 29 of 44 eyes (66%) demonstrated false-positive scans. Our inclusion criteria are relevant to the age demographic that commonly presents with epiphora. The technique of interpretation is comparable to that of other authors who have previously reported HCT (*8,9*). We add further assessment of patients in the form of qualitative analysis and quantitative postlacrimal massage data that have not previously been reported in the literature.

Qualitative studies of dacryoscintigraphy have been reported for presac, sac, and duct delay, citing a positive scintigraphy rate of 11%–13%, 35%–52%, and 17%–37%, respectively (*3,4,12,15,16*) for patients with epiphora with patent lacrimal syringing and absence of lid or ocular surface pathology. These qualitative studies were on patients with a mean age range of 54.6–64.6 y, used ^{99m}Tc-pertechnetate, and are therefore more comparable to our cohort than were previous quantitative studies. Our study of asymptomatic participants revealed a false-positive dacryoscintigraphy scan rate of 66%. The distribution rate of false-positive scans in our study showed delay in 6 of 44 presac scans (14%) and 23 of 44 postsac scans (52%). In a study of symptomatic patients, a similar rate was found in a study by Peter and Pearson, quoting a presac delay rate of 11%, a sac delay rate of 52%. and a duct delay rate of 37% in symptomatic patients (*4*). The distribution of false-positive dacryoscintigraphy findings in our study, roughly a 1:4 difference in frequency between presac and postsac scans, is equivalent to that of Peter and Pearson's study.

The high rate of false-positive dacryoscintigraphy studies in our cohort suggests a low specificity for this investigation or possibly a high rate of subclinical lacrimal drainage pathology, which cannot be excluded without additional techniques such as dacryocystography or MR dacryocystography. Because we demonstrated a high degree of symmetry in the false-positive cases on qualitative and quantitative analysis, there is likely value in bilateral testing in the clinical evaluation of a patient with unilateral epiphora.

PLM

Qualitative Assessment. We found that the addition of nose blowing and lid massage resulted in a high rate of reversal in apparent drainage delay on qualitative assessment—79% of false-positive results averted. The mechanism for this reversal is unclear, as the value of dacryoscintigraphy emphasizes assessing normal function with blinking.

Movement of tears into the nasolacrimal sac is an active process that occurs during the act of blinking. When the eyelid is shut, the lid component of the orbicularis oculi muscle shortens and compresses the canaliculi. The orbital part of the orbicularis oculi pulls the sac laterally, creating a negative pressure within the sac. The combined action results in tears being drawn into the sac. When the lid is opened, the pressure within the sac is restored. This active mechanism is known as the lacrimal pump. Once in the sac, the tears transit down the duct passively into the nasal cavity.

It is possible that the act of circular lid massage activates lacrimal pump action, facilitating transit of tears. The improvement may suggest a subclinical canalicular or postsac stenosis. This was a study of healthy participants; thus, the normalization of a significant proportion after massage raises the possibility of improved test specificity with this technique. As such, our study suggests that lacrimal massage and nose blowing perhaps should be performed routinely, particularly if used as the single investigation for epiphora workup. Of note, the improvement in our study was noted in only 1 participant after nose blowing and involved the postsac region of both eyes. Thus, the improvement in test specificity is likely to represent predominantly the effect of the lid massage. There are currently no data on lid massage or nose blowing improvement that may occur in nasolacrimal duct stenosis or functional obstruction. Hence, further studies are required to delineate the place of this technique and define its role in improving specificity.

Quantitative Assessment. The PLM HCTs were noted to be markedly higher than the NLM HCTs. The difference was statistically significant for the presac region. Judging from the time–activity curves generated, this may be an indication of a plateauing of clearance rate by the time the PLM scans were performed, which was nearly an hour after the instillation of the radiotracer. In our opinion, the markedly higher PLM HCT is of doubtful clinical value. PLM appears to have utility only for qualitative evaluation.

CONCLUSION

The normative dacryoscintigraphy HCTs of the presac and whole-eye regions in an older asymptomatic population with no detectable lid or lacrimal pathology are presented in this study. Judging from our secondary qualitative endpoints, it would appear that there is a low specificity of dacryoscintigraphy for the age demographic, comparable to the usual population that presents with epiphora. Hence, we believe there are significant limitations for dacryoscintigraphy as a solitary investigation for epiphora when the clinical examination shows normal findings. Dacryoscintigraphy may have more value as a test of function in conjunction with dacryocystography. Standardization of techniques and delineation of normative quantitative values will assist clinicians in scan interpretation, which is addressed by the presac and whole-eye HCTs derived from

our normative data. The specificity of the study would appear to be significantly improved by the addition of lid massage, and this technique merits further research.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: What are the normal HCTs of a radiotracer when dacryoscintigraphy is being interpreted in older patients?

PERTINENT FINDINGS: The normal HCTs for the presac and whole-eye regions were identified in a cohort of asymptomatic participants with no detectable lid or lacrimal dysfunction in the age group that commonly presents with epiphora. A high false-positive rate was noted. A significant proportion of false-positive findings were averted with the addition of lid massage.

IMPLICATIONS FOR PATIENT CARE: The reference ranges of HCT identified in this study may help in the interpretation of dacryoscintigraphy in identifying presac and postsac functional obstruction in older patients presenting with epiphora. The addition of lid massage to the imaging protocol appears to reduce the chances of a false-positive finding.

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