Research letter

An 18-year retrospective study on the outcomes of keratoacanthomas with different treatment modalities at a single academic centre

DOI: 10.1111/bjd.15225

Dear Editors, The clinical course for keratoacanthomas (KAs) varies from self-resolving to invasive cancers.[1,2] KA is often treated with surgical intervention,[2,3] but other treatments such as electrodessication and curettage,[4] cryotherapy,[4] topical medications,[2,5] intralesional chemotherapy,[2] acitretin[2] and active surveillance[6] have been employed. Randomized controlled studies of different treatment modalities are lacking. The largest systematic review consisted of 113 case reports and case series (445 patients included) and reported 18 recurrent or persistent KA cases (4%),[2] but this data is prone to publication bias, as unusual cases are more likely to be reported and treatment outcomes could not be directly compared.

Our study examines KA recurrence and persistence rates of different treatment approaches at a single institution. After Institutional Review Board approval, we searched the Stanford Cancer Institute Research Database from January 1998 to February 2016 using the keywords 'keratoacanthoma', 'crateriform' or 'cup-shaped' and applied the following two inclusion criteria: (i) at least one KA-positive biopsy read by a Stanford dermatopathologist and (ii) at least one dermatology visit documenting treatment of KAs. After manual chart review, 261 patients (with 363 KAs) met these criteria (Fig. 1). 'Recurrence' was defined as regrowth of treated lesions documented as no clinically visible lesion after first treatment approach (FTA). 'Persistence' was defined as lesions clinically visible at the same anatomic location after FTA.

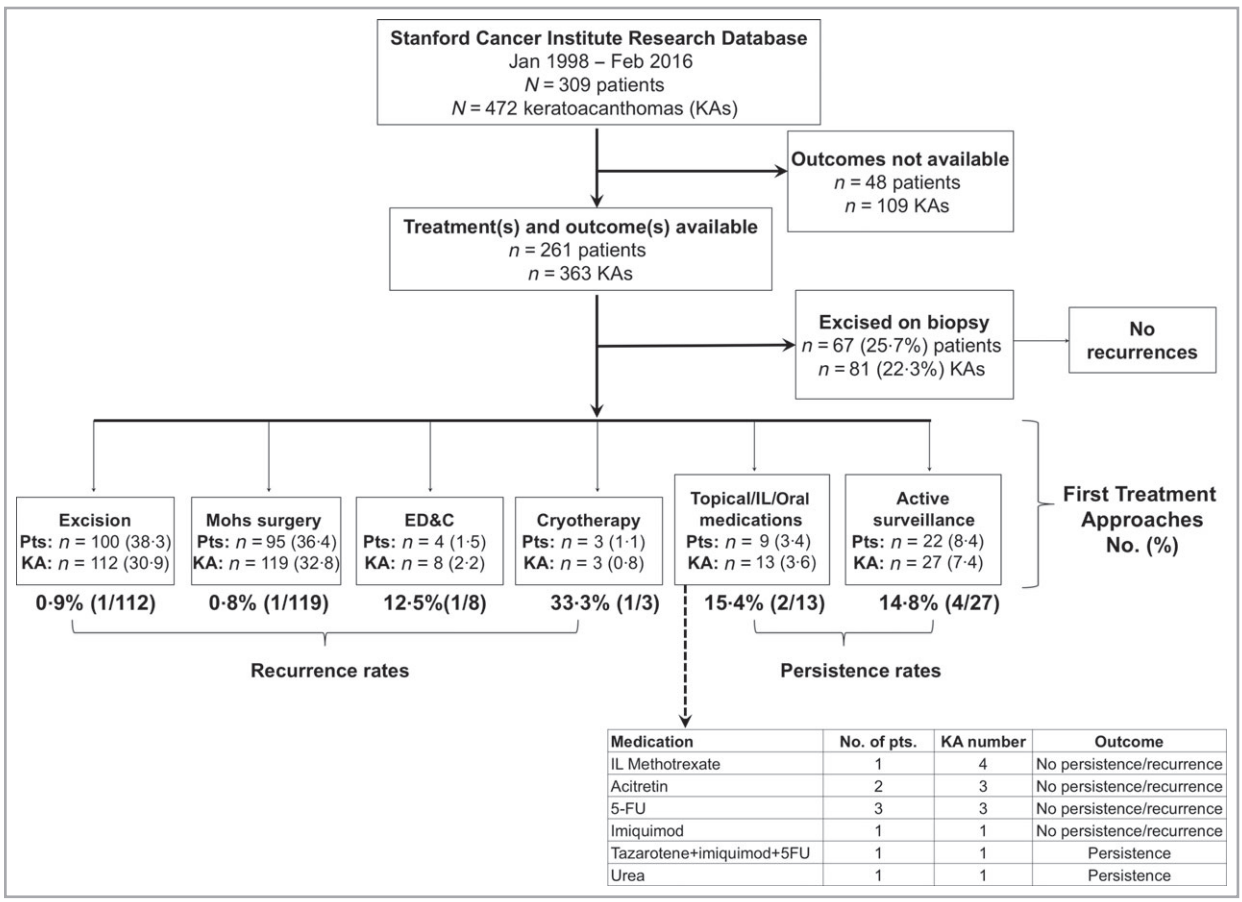

Fig. 1. Flowchart of the study. ED&C, electrodessication and curettage; 5-FU, 5-fluorouracil; IL, intralesional; Pts, patients.

Table 1 Time to recurrence and duration of persistence after the first treatment approach for recurrent and persistent keratoacanthomas (KAs), respectively, at Stanford, compared with our tabulation of Savage *et al.* systematic review (2013)

	Number of KAs		Months to KA recurrence		Months of KA persistence before initiation of second treatment	
First treatment approach	Stanford (consecutive cases)	Savage *et al.*	Stanford[a]	Savage *et al.*	Stanford[b]	Savage *et al.*
Mohs surgery	1	1	3	2	None	None
Excision	1	9	7·5	2 (0·5–12·0)		
Electrodessication and curettage	1	2	1·5	1·6 (0·25–3·0)		
Cryotherapy	1	0	Not available	None		
IL/topical/oral medications	2	3	None	3 (recurrence, n = 1)	9·8 (8·2–11·3)	9·75 (1·5–18) (persistence, n = 2)
Active surveillance	4	1		None	4·1 (3·8–5·7)	29
Total, median (range)	10	16[c]	3 (1·5–7·5)	2 (0·25–12·0)	5 (3·8–11·3)	18 (1·5–29·0)

IL, intralesional. [a]Calculated from the date of the first procedure (Mohs surgery, excision or electrodessication and curettage) to the date of the recurrence. [b]Calculated from the date of first treatment initiation to the date of second treatment (which were either Mohs surgery or excision). [c]The 2013 systematic review by Savage *et al.* reported 18 recurrent/persistent cases. However, upon re-examination of individual cases, we determined that two cases (reported by Calonje *et al.* and Schwartz *et al.*) did not meet our definitions of recurrence/persistence and were thus excluded. Median and range are reported where there are more than two KA cases. All recurrent and persistent KAs reported here subsequently underwent excision or Mohs surgery with 100% resolution at follow-up.

Average age at KA diagnosis was 73 years (SD 11·7). Median follow-up time was 2·3 years (range 0–17·9). Overall resolution rate of KA was 97·2% (353 of 363 KAs) after the FTA, with 2·8% either recurring [four of 363 KAs (1·1%)] or persisting [six of 363 KAs (1·7%)]. The median size of resolved and recurring/persisting KAs was 1·0 cm (range 0·3–4·5) and 1·1 cm (range 0·4–1·6), respectively. There was no significant difference in age, sex, race and immunosuppression status between individuals with KAs that resolved after the FTA (n = 251 patients) and those whose KAs did not (n = 10 patients). Of the 21 patients who were immunosuppressed, 20 experienced KA resolution after FTA and one did not.

Surgical treatment by excision or Mohs surgery led to significantly lower recurrence rates (< 1%) than nonsurgical treatments, whose recurrence or persistence rates ranged from 12·5% to 33·3% (Fig. 1).

To assist with patient counselling and estimation of duration needed for monitoring KAs, time to recurrence and duration of persistence after the FTA are shown in Table 1. Median time to recurrence was 3 months (range 1·5–7·5) when all treatment modalities were considered. Median persistence time for persistent KAs prior to initiation of second treatment approach (STA) was 5 months (range 3·8–11·3). All recurrent and persistent KAs resolved after the STA, which was either Mohs surgery (n = 5) or excision (n = 5). No metastatic KA cases were found.

Median time to resolution for KAs after nonsurgical FTAs were as follows: active surveillance was 3 months (range 0·6–17, n = 23), cryotherapy was 1·4 months (range 1·2–1·7, n = 2), electrodessication and curettage was 3 months (range 1·7–5·0, n = 7) and medications (topical, intralesional or oral) was 6 months (range 1·6–12·6, n = 11).

Our data provides a single-site source of recurrence and persistence rates of KAs treated with a variety of FTAs (Fig. 1). Although direct comparison of our data with prior systematic reviews is difficult owing to differences in methodology, differences between our data and the largest systematic review[2] to date are shown in Table 1. Our median persistence duration of KA after FTA [median 5 months (range 3·8–11·3), n = 6] was different from the median persistence time after FTA in the Savage *et al.* systematic review [18 months (range 1·5–29·0), n = 3], although the sample size was small. Savage *et al.* also reported that four of 16 patients required more than two treatments, while none of 261 patients at Stanford required more than two treatments.

Compared with a previous study of 43 KAs treated with Mohs surgery,[3] KA recurrence after Mohs surgery was threefold lower (2·4% vs. 0·8%). While the number of patients with KA treated with cryotherapy is small, our resolution rate was only 67%, lower than a prior expert opinion of 99%.[4] Lastly, KAs treated with nonsurgical approaches including active surveillance can take up to 1 year to resolve. Hence, KAs persisting after 1 year would be candidates for surgical removal, although multicentre studies are needed to establish optimal duration for expectant management.

Despite our retrospective study being the largest single-site study to date, limitations include lack of multivariate analysis owing to low sample size, and nonrandomized nonblinded design.

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Funding sources: D.C.T. was supported by the Stanford Medical Scholars Research Program. Stanford Cancer Research Database was supported in part by National Cancer Institute Cancer Center Support Grant 5P30CA124435 and Stanford National Institutes of Health/National Center for Research Resources Clinical and Translational Science Awards award number UL1 RR025744.

Conflicts of interest: A.L.S.C. is a clinical investigator for studies sponsored by Merck, Genentech and Novartis. No funding/sponsor was involved in study design, data collection, analysis and interpretation, and writing of the manuscript. The study was approved by the Stanford Institution Review Board.