

# Skin conditions in liver transplant recipients in a Singapore academic medical center: A retrospective cohort study



Bertrand ShengYang Lian, MBBS, MRCP,<sup>a</sup> Thinesh Lee Krishnamoorthy, MBChB, MRCP,<sup>b,c</sup> and Choon Chiat Oh, MBBS, MSc, MCI, FRCP<sup>a,c</sup>  
*Singapore*

**Background:** Liver transplant recipients are at lifelong risk of immunosuppression-related cutaneous complications, such as malignancy and infection.

**Objective:** Our study aims to assess the epidemiology of dermatologic conditions among liver transplant recipients in an academic medical center in Singapore.

**Methods:** Medical records of liver transplant recipients on follow-up with gastroenterology and dermatology departments at the Singapore General Hospital between 2006 and 2021 were retrospectively reviewed. A literature review was subsequently performed on the keywords “liver transplant” and “dermatology.”

**Results:** A total of 99 liver transplant recipients were identified in this study. Sixty-nine patients (70%) had at least 1 dermatologic condition. Inflammatory skin conditions were the most common (53%), followed by cutaneous infection (36%) and benign cutaneous tumors (30%). Malignant and premalignant lesions were the least common skin conditions reported (10%). Our study results concurred with many other studies reported worldwide, demonstrating a low cutaneous malignancy burden after liver transplantation.

**Limitations:** The study included a small population size in a single center and did not have a pre-existing protocol for pretransplant dermatologic surveillance.

**Conclusion:** Although the incidence of skin cancer after liver transplant in Singapore is low, the patients will benefit from long-term dermatology surveillance, given the long-term risks of infection and malignant skin conditions. (JAAD Int 2021;4:70-8.)

**Key words:** actinic keratosis; basal cell carcinoma; Bowen disease; cutaneous malignancy; dermatology; infection; liver transplant; tinea infection; transplant.

## INTRODUCTION

The demand for liver transplantation in Singapore far exceeds the availability of liver organs. The incidence of liver transplantation has increased, reaching an average of 38 cases per year between 2015 and 2019, compared with an average of 25 cases

per year in the preceding 5 years.<sup>1</sup> The increase in the number of transplants is likely a reflection of ongoing legislation facilitating organ harvesting, changing cultural attitudes toward organ donation, improving the socioeconomic status of citizens, and advancing skill and technology in liver surgery.<sup>2,3</sup>

From the Department of Dermatology<sup>a</sup> and Department of Gastroenterology and Hepatology, Singapore General Hospital<sup>b</sup>; and DUKE-NUS Medical School.<sup>c</sup>

Funding sources: None.

IRB approval status: Not applicable.

Conflicts of interest: None disclosed.

Accepted for publication June 26, 2021.

Correspondence to: Choon Chiat Oh, MBBS, MSc, MCI, FRCP, Department of Dermatology, Singapore General Hospital,

Outram Road, Singapore 169608. E-mail: [oh.choon.chiat@singhealth.com.sg](mailto:oh.choon.chiat@singhealth.com.sg).

2666-3287

© 2021 by the American Academy of Dermatology, Inc. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.jdin.2021.06.002>

With the increase in liver transplants, there is a growing concern for cutaneous malignancies and infections as long-term complications of immunosuppression. Although posttransplant cutaneous malignancy has been well documented in kidney transplant recipients, similar complications are not widely reported in liver transplant recipients.<sup>4</sup>

Incidence rates of cutaneous malignancy in Western populations vary widely, depending on the geographic region and duration of follow-up.<sup>5-9</sup> Epidemiologic data for such complications in the Asian population are limited. Our study aims to assess the epidemiology of dermatologic conditions among liver transplant recipients in the largest academic medical center in Singapore. We have also performed a review of the existing literature to date.

## METHODS

### Patients

The medical records of liver transplant recipients on follow-up with gastroenterology and dermatology departments at the Singapore General Hospital between January 1, 2006, and January 1, 2021 were reviewed. Patients were included if they had a follow-up of at least 1 year and were subject to annual skin examination by a dermatologist. The frequency of dermatologic evaluation was adjusted, depending on the presence or absence of significant findings. Dermatologic diagnoses, including relevant histologic and microbiologic investigations, were recorded. Other collected data included age, sex, ethnicity, primary liver disease, type of donor organ transplant, time after transplantation, and immunosuppressive regime.

### Immunosuppression

All patients were followed up by the liver transplant team, and immunosuppression was adjusted as required. Primary induction immunosuppression consisted of tacrolimus (or cyclosporine if there was contraindication or toxicity to tacrolimus), mycophenolate mofetil, and prednisolone. Mycophenolate mofetil and prednisolone were reduced over time and withdrawn where possible. Patients were subsequently maintained on tacrolimus or cyclosporine monotherapy unless concomitant immunosuppression was required.

## Literature review

A literature search in PubMed, MEDLINE, and Cochrane databases was performed in March 2021 to identify original articles written in English. Search terms used the keywords “liver transplant” and “dermatology.” Titles and abstracts were screened, and studies deemed relevant underwent full-text article assessment. Inclusion criteria were published observational studies including cross-sectional and cohort studies documenting the frequency of dermatologic conditions in liver transplant patients. References of all selected studies were also examined.

## RESULTS

### Study

A total of 140 liver transplant recipients were identified. Of these, 99 recipients were included in the study (26 died before the dermatologic consult, and 15 were not seen by the dermatology). The general characteristics of recipients are summarized in [Table I](#).

The population consisted of 67 (68%) men and 32 (32%) women. The mean age at transplantation was  $57.7 \pm 7.2$  years. In terms of ethnicity, 82 (83%) were Chinese, 10 (10%) were Malay, 5 (5%) were Indian, and 2 (2%) were of other ethnicities. Thirty-three (33%) were followed for more than 10 years, 26 (26%) for 6 to 10 years, and 40 (40%) for less than 5 years. The mean duration of follow-up was  $7.4 \pm 4.1$  years (range, 1.8-15 years).

The most common etiology of liver disease was hepatitis B (43%), followed by nonalcoholic steatohepatitis (16%) and primary biliary cholangitis (16%). Other etiologies included cryptogenic (8%), hepatitis C (4%), and alcohol-related (4%) and drug-related (3%) liver disease. Twenty-seven (27%) patients had hepatocellular carcinoma before transplant, of whom 15 (15%) were related to hepatitis B, 6 (6%) were related to nonalcoholic steatohepatitis, and the remainder were related to other etiologies. Of these patients, 76 (77%) received deceased donor liver transplants, whereas 23 (23%) received living donor liver transplants.

Seventy-eight (79%) patients were found to have a dermatologic diagnosis during follow-up, with the findings summarized in [Table II](#). Inflammatory skin diagnoses were most commonly seen (53%) and included eczema, seborrheic dermatitis, seborrheic hyperplasia, acne, erythema nodosum, psoriasis, chronic urticaria, rosacea, and macular amyloidosis.

## CAPSULE SUMMARY

- The incidence of skin cancer after liver transplant is low in this Asian cohort, concurring with epidemiologic data worldwide.
- In our cohort, inflammatory skin conditions were most common after liver transplant, followed by cutaneous infection and benign cutaneous tumors.

**Abbreviation used:**

HPV: human papillomavirus

Skin infection was the next most common etiology, accounting for 36% of the patients. Thirty (30%) patients had benign skin lesions and 10 (10%) had premalignant or malignant lesions.

Viral warts were the most common skin infection (14%; n = 14). The duration from transplant did not appear to influence the development of warts, as they were diagnosed throughout the follow-up period (mean duration after transplant to the diagnosis of warts:  $6.8 \pm 3.63$  years). In terms of location, the warts were predominantly found in the head and neck region (Table III).

Other skin infections seen included fungal infections (8%; n = 8) (tinea infection [4%, n = 4], onychomycosis [3%; n = 3], and pityriasis versicolor [1%; n = 1]), folliculitis (5%, n = 5), herpes simplex infections (3%, n = 3), cutaneous abscesses (2%, n = 2), intertrigo (2%, n = 2), erysipelas (1%, n = ), and ecthyma (1%, n = 1). These infections were more prevalent in the first 5 years after transplant.

Four (4%) cases of cutaneous malignancies were seen in our cohort. This consisted of basal cell carcinoma (n = 1) and Bowen disease (n = 3). There were 6 (6%) cases of actinic keratosis, and 80% of these lesions were found in the sun-exposed areas. The mean duration after transplant to the diagnosis of malignant/premalignant lesions was  $8.1 \pm 3.96$  years. All malignancies and premalignancies were treated surgically or with cryotherapy. Details are summarized in Table IV.

**Literature review**

The initial literature search identified 131 articles, which was then expanded to 140 articles after screening the references. Based on our criteria, a total of 9 studies were selected, of which 3 were prospective and 6 retrospective. A summary of the relevant information from these articles is presented in Table V.<sup>5-13</sup>

A total of 10,193 patients were described in the articles, of which 6277 were men and 3516 were women. The sex of 400 patients was not specified. The mean duration from liver transplant was reported to range from 3 to 9 years.

The incidence of cutaneous malignancy reported in these articles (ranged from 0.8% to 48%). The pooled cumulative incidence of cutaneous malignancy from all included studies was 2.8%. When

**Table I.** Biodata of liver transplant recipients

Characteristic	No. (%)
Patients	99
Age (years)	
Mean $\pm$ SD	57.7 $\pm$ 7.2 years
20-40	3 (3)
41-60	59 (60)
61-80	37 (37)
Sex	
Male	67 (68)
Female	32 (32)
Ethnicity	
Chinese	82 (83)
Malay	10 (10)
Indian	5 (5)
Others	
German	1 (1)
Bangladeshi	1 (1)
Type of donor	
Deceased donor liver transplant	76 (77)
Living donor liver transplant	23 (23)
Etiology of liver failure	
Hepatitis B	43 (43)
Nonalcoholic steatohepatitis	16 (16)
Primary biliary cholangitis	16 (16)
Cryptogenic	8 (8)
Hepatitis C	4 (4)
Alcohol	4 (4)
Drug	3 (3)
Others	5 (5)
Hepatocellular carcinoma	
Total	27 (27)
Hepatitis B related	15 (15)
Nonalcoholic steatohepatitis related	6 (6)
Others	6 (6)
Immunosuppression	
Prednisolone	98 (99)
Hydrocortisone	1 (1)
Tacrolimus	89 (90)
Cyclosporine	10 (10)
Mycophenolate mofetil	90 (91)
Everolimus	2 (2)
Treatment duration (years)	
<5	40 (40)
5-10	26 (26)
>10	33 (33)

reported, cutaneous malignancy was more frequent 3 years after transplantation, with a mean duration of 5.1 years from transplant. The cumulative incidence of cutaneous malignancy for studies with up to 3 years of follow-up was 1.1%, whereas the incidence was 10.8% when restricted to studies with at least 5 years of follow-up.

**Table II.** Dermatologic diagnosis during follow-up

Dermatologic diagnosis	No. of patients (%)
Malignant/premalignant	10 (10)
Basal cell carcinoma	1 (1)
Squamous cell carcinoma	0
Melanoma	0
Bowen disease	3 (3)
Actinic keratosis	6 (6)
Infection	36 (36)
Warts	14 (14)
Folliculitis	5 (5)
Fungal infections:	
Tinea infection	4 (4)
Onychomycosis	3 (3)
Pityriasis versicolor	1 (1)
Herpes simplex virus	3 (3)
Abscess	2 (2)
Intertrigo	2 (2)
Erysipelas	1 (1)
Ecthyma	1 (1)
Benign lesions	30 (30)
Seborrheic keratosis	21 (21)
Cysts	3 (3)
Nevi	5 (5)
Angioleiomyoma.	1 (1)
Inflammatory conditions	52 (53)
Eczema	29 (29)
Seborrheic dermatitis	8 (8)
Seborrheic hyperplasia	7 (7)
Acne	3 (3)
Erythema nodosum	1 (1)
Psoriasis	1 (1)
Chronic urticaria	1 (1)
Rosacea	1 (1)
Macular amyloidosis	1 (1)

Findings determining whether specific immunosuppression regimes affect cutaneous malignancy were inconclusive, and reporting was variable. Belloni-Fortina et al<sup>5</sup> reported a significant association between cyclosporine and cutaneous malignancy when compared with tacrolimus, whereas Ducroux et al<sup>7</sup> reported no significant association when using either cyclosporine or tacrolimus.

Opportunistic infections were also reported in 3 articles with a cumulative incidence of 48% and 8.7% for tinea infection and viral warts, respectively.

## DISCUSSION

Only 4 of 100 patients in our study developed a cutaneous malignancy over 10 years. Such an incidence rate is low and comparable with the pooled

incidence rates of the studies mentioned in our review.<sup>5-13</sup> Of note is the high incidence of viral warts in our liver transplant population.

The cumulative incidence of cutaneous malignancies seen in the literature review was significantly higher with follow-up durations of more than 5 years. This likely reflects the impact of longer durations of immunosuppression and older age (>60 years), both of which are known risk factors.<sup>5,7,14</sup> Other established risk factors include prolonged exposure to UV light and a lighter skin phototype, which likely accounts for the high incidence of skin cancer in Australian and French cohorts.<sup>6,7,9,12</sup> Protective factors in our study cohort include a darker skin phenotype (Fitzpatrick 3 and 4) and a younger age at transplant. Nonetheless, given the lifelong immunosuppression for liver transplant patients, health practitioners must remain vigilant in their surveillance for skin cancer and continue to emphasize the importance of sun protection.

Viral warts are the most common cutaneous infection in our study, which is consistent with the earlier studies.<sup>5,8,10</sup> The warts were predominantly found in the sun-exposed head and neck region, consistent with an earlier study performed on our renal transplant patients.<sup>15</sup> Viral warts, while benign, can be difficult to treat in an immunosuppressed patient. Not only are such warts highly prevalent in organ transplant recipients but also they have low spontaneous regression rates and can be resistant to standard treatment.<sup>16-18</sup> Timely treatment is important as they can negatively impact the quality of life if they persist or recur.<sup>19</sup>

While certain strains of human papillomavirus (HPV) are known risk factors for the development of anogenital cancer, their role in cutaneous squamous cell carcinoma has yet to be well established.<sup>20-22</sup> Nonetheless, there is a growing appreciation of the role that HPV plays in cancer initiation via enhanced UV carcinogenicity, impairment of DNA repair, and abnormal cellular apoptosis.<sup>23-26</sup> Based on the British Association of Dermatologists guidelines, established therapy for viral warts includes topical destructive agents, virucidal and antiproliferative agents, retinoids, and immunologic therapy.<sup>27</sup> A novel and less invasive treatment modality for viral warts is the use of the HPV vaccine for immune stimulation. This has been shown to reduce cutaneous viral warts in at least 70% of treated patients.<sup>28</sup> Taking this one step further, case reports have also suggested the use of the HPV vaccine in the chemoprevention of keratinocyte cancers and even in the treatment of squamous cell carcinoma.<sup>29</sup> The use of

**Table III.** Details of cutaneous infections in the liver transplant cohort

Diagnosis	Time after transplant; No. of patients (%)	Location; No. of patients (%)	
Warts*	<5 years; 5 (42)	Upper limbs; 2 (17)	Sun exposed; 10 (83)
	5-10 years; 4 (33)	Lower limbs; 2 (17)	Non-sun exposed; 2 (17)
	>10 years; 3 (25)	Generalized; 2 (17)	
		Head and neck; 5 (42)	
		Genital; 1 (8)	
Fungal infection (tinea/ onychomycosis/pityriasis versicolor)	<5 years; 6 (75)		
	5-10 years; 2 (25)		
	>10 years; 0		
Folliculitis	<5 years; 3 (60)		
	5-10 years; 1 (20)		
	>10 years; 1 (20)		

\*Two patients with incomplete data.

**Table IV.** Details of cutaneous malignancies in the liver transplant cohort

Cancer/precancer type	Time after transplant; No. of patients (%)	Location; No. of patients (%)	Immunosuppressive agents >6 months; No. of patients
Basal cell carcinoma	<5 years; 0	Sun exposed; 0	Tacrolimus; 1
	5-10 years; 1 (100)	Non-sun exposed; 1 (100)	Mycophenolate mofetil; 0
	>10 years; 0		Prednisolone; 0
Bowen disease	<5 years; 1 (33)	Sun exposed; 2 (67)	Tacrolimus; 3
	5-10 years; 2 (67)	Non-sun exposed; 1 (33)	Mycophenolate mofetil; 3
	>10 years; 0		Prednisolone; 2
Actinic keratosis	<5 years; 1 (17)	Sun exposed; 6 (100)	Tacrolimus; 6
	5-10 years; 2 (33)	Non-sun exposed; 0	Mycophenolate mofetil; 5
	>10 years; 3 (50)		Prednisolone; 3
			Cyclosporine; 1

the HPV vaccine for the prevention and treatment of keratinocyte carcinoma is a promising undertaking that should be further studied.

Immunosuppressive agents are postulated to decrease the potency of innate antitumor immune reactions, blunt antineoplastic surveillance mechanisms, and impair immunity against copathogenic viruses.<sup>30</sup> Conversion to alternative immunosuppressants or dose reduction is considered when faced with recurrent life-threatening malignancy or recalcitrant viral warts. Although data are limited, a literature review by Brennan et al<sup>31</sup> has suggested potential antiviral mechanisms for mammalian target of rapamycin inhibition of HPV. There have been reports of successful clearance of treatment-resistant viral warts through the withdrawal of calcineurin inhibitors and conversion to a mammalian target of rapamycin inhibitor.<sup>32,33</sup> Use of low-dose immunosuppression has also been shown to result in significantly fewer malignancies in renal transplant patients, with no significant impact on overall graft survival or patient mortality, albeit with

higher frequencies of graft rejection.<sup>34</sup> No studies exploring this as a therapeutic consideration have been performed for liver transplant recipients. This is likely because renal replacement therapy is readily available for kidney transplant recipients experiencing graft failure but not for liver transplant recipients. With the advent of modern immunosuppression and improved graft survival, attention should be turned to addressing the associated morbidity and mortality of immunosuppression. Although the risks of graft failure may be onerous, measures such as switching immunosuppressants or dose reduction may be worth considering in patients with aggressive skin cancers or recalcitrant viral warts.

Limitations of our study include a small population size in a single centre. Moreover, 15% of the transplant patients were not examined by the dermatologists. There was also no pre-existing protocol for pretransplant dermatologic surveillance, which meant that patients could have had unidentified pre-existing lesions.

**Table V.** Summary of skin conditions in liver transplant cohorts worldwide

Author; country; study period	Study type; size; age at transplant; sex (male: female); duration after transplant	Diagnoses	
Otley et al <sup>11</sup> ; United States; 1996-2001 (6 years)	Retrospective; 8075 patients; age not mentioned; 5141 (64%); 2934 (36%); median: 3 years	Malignant/premalignant Skin cancer: 1.1%	
Sarac et al <sup>10</sup> ; Turkey; 2019	Prospective; 520 patients; mean age: 44.2 ± 18.2 years; 357 (69%); 163 (31%); mean: 3 years	Malignant/premalignant Skin cancer: 0.8% Squamous cell carcinoma: 0.6% Basal cell carcinoma: 0.2% Actinic keratosis: 13.8% Infection Tinea infection: 60.4% Viral warts: 4.8% Herpes infection: 2.9%	Inflammatory Acne: 11.7% Contact dermatitis: 7.9% Others Xerosis: 47.5% Hyperpigmentation: 26.9% Seborrheic keratosis: 20.3% Haemangioma: 9.2% Sebaceous hyperplasia: 8.5% Spider angioma: 5.4% Palmoplantar hyperkeratosis: 2.9% Alopecia: 2%
Ducroux et al <sup>7</sup> ; France; 1996-2008 (13 years)	Retrospective; 371 patients; mean age: 51.3 years; 243 (65%); 128 (35%); mean: 8.2 years	Malignant/premalignant Skin cancer: 13.5% Squamous cell carcinoma: 5.7% Basal cell carcinoma: 17.8% Bowen disease: 1.6% Actinic keratosis: 3.5% Melanoma: 1.3% Atypical fibroxanthoma: 0.3% Kaposi sarcoma: 0.3%	
Cohen et al <sup>6</sup> ; United States; 2005-2013 (9 years)	Retrospective; 370 patients; mean age: 59.8 ± 10.2 years; 223 (60%); 147 (40%); mean: 7.9 years	Malignant/premalignant Skin cancer: 3.2% Squamous cell carcinoma: 2.4% Basal cell carcinoma: 1%	
Ashraf et al <sup>12</sup> ; United States; 2010-2019 (10 years)	Retrospective; 300 patients; age, sex, and follow-up not mentioned	Malignant/premalignant Skin cancer: 6.7% Squamous cell carcinoma: 3.7% Basal cell carcinoma: 3% Actinic keratosis: 3.3%	

Continued

Table V. Cont'd

Author; country; study period	Study type; size; age at transplant; sex (male: female); duration after transplant	Diagnoses
Iannaccone et al <sup>9</sup> ; Australia; 2016	Retrospective; 208 patients; mean age 55 ± 13 years; 133 (64%): 75 (36%); mean: 9 years	Malignant/premalignant Skin cancer: 25% Squamous cell carcinoma: 9% Basal cell carcinoma: 10% Bowen disease: 13% Actinic keratosis: 83%
Belloni-Fortina et al <sup>5</sup> ; Italy; 1987-2006 (20 years)	Prospective; 161 patients; mean age: 47.4 ± 11.0 years; 116 (72%): 45 (28%); mean: 6 years	Malignant/premalignant Skin cancer: 8.7% Squamous cell carcinoma: 3.7% Basal cell carcinoma: 3.7% Kaposi sarcoma: 1.9% Bowen disease: 1.9% Melanoma: 0.6% Infection Viral warts: 18.6% Mycotic intertrigo: 13% Pityriasis versicolor: 6.2% Folliculitis: 5% Onychomycosis: 3.7% Tinea corporis: 3.1% Herpes simplex: 1.9% Herpes zoster: 1.9% Inflammatory Acne: 7.4% Seborrheic dermatitis: 5% Seborrheic hyperplasia: 3.7% Others Xerosis: 28.6% Hypertrichosis: 18.6% Atrophy: 14.2% Telangiectasia: 14.2% Alopecia: 4.3%
Perera et al <sup>8</sup> ; United Kingdom; 2006	Prospective; 100 patients; median age: 42.5 years; sex not mentioned; mean: 5.5 years	Malignant/premalignant Skin cancer: 4% Squamous cell carcinoma: 1% Basal cell carcinoma: 3% Bowen disease: 4% Actinic keratosis: 11% Infection Tinea infection: 19% Viral warts: 13% Folliculitis: 4% Molluscum: 1% Herpes simplex virus: 1% Erythrasma: 1%
Ge et al <sup>13</sup> ; Australia; 2011-2016 (6 years)	Retrospective; 88 patients; median age: 64 years; 64 (73%): 24 (27%); mean: 3.6 years	Malignant/premalignant Skin cancer: 47%

## CONCLUSION

In summary, although the skin cancer burden in liver transplant recipients is low in Singapore (a predominantly Asian cohort), control of viral wart infections remains a key area of need. Moving forward, a long-term dermatology follow-up should be routine for all liver transplant recipients, in view of the wide spectrum of skin conditions faced by liver transplant recipients. As shown in this study, these include skin cancers, opportunistic skin infections (warts, fungal, and bacterial infections), and inflammatory skin conditions (eczema, sebaceous hyperplasia, and acne). These conditions are best managed by dermatologists. Future studies on larger cohorts will also be needed to better document the epidemiology of the cutaneous disease in Asia.

## Conflicts of interest

None declared.

## REFERENCES

1. Number of liver transplants performed in Singapore from 2010-2020. Live On. Accessed March 23, 2021. <https://www.liveon.gov.sg/>
2. Hibi T, Wei Chieh AK, Chi-Yan Chan A, Bhangui P. Current status of liver transplantation in Asia. *Int J Surg*. 2020;82S:4-8. <https://doi.org/10.1016/j.ijsu.2020.05.071>
3. Low HC, Da Costa M, Prabhakaran K, et al. Impact of new legislation on presumed consent on organ donation on liver transplant in Singapore: a preliminary analysis. *Transplantation*. 2006;82(9):1234-1237. <https://doi.org/10.1097/01.tp.0000236720.66204.16>
4. Matinfar M, Shahidi S, Feizi A. Incidence of nonmelanoma skin cancer in renal transplant recipients: a systematic review and meta-analysis. *J Res Med Sci*. 2018;23:14. [https://doi.org/10.4103/jrms.JRMS\\_817\\_17](https://doi.org/10.4103/jrms.JRMS_817_17)
5. Belloni-Fortina A, Piaserico S, Bordignon M, et al. Skin cancer and other cutaneous disorders in liver transplant recipients. *Acta Derm Venereol*. 2012;92(4):411-415. <https://doi.org/10.2340/00015555-1316>
6. Cohen BE, Krivitskiy I, Bui S, et al. Comparison of skin cancer incidence in Caucasian and non-Caucasian liver vs. lung transplant recipients: a tale of two regimens. *Clin Drug Investig*. 2019;39(2):197-203. <https://doi.org/10.1007/s40261-018-0732-3>
7. Ducroux E, Boillot O, Ocampo MA, et al. Skin cancers after liver transplantation: retrospective single-center study on 371 recipients. *Transplantation*. 2014;98(3):335-340. <https://doi.org/10.1097/TP.0000000000000051>
8. Perera GK, Child FJ, Heaton N, O'Grady J, Higgins EM. Skin lesions in adult liver transplant recipients: a study of 100 consecutive patients. *Br J Dermatol*. 2006;154(5):868-872. <https://doi.org/10.1111/j.1365-2133.2006.07154.x>
9. Iannacone MR, Sinnya S, Pandeya N, et al. Prevalence of skin cancer and related skin tumors in high-risk kidney and liver transplant recipients in Queensland, Australia. *J Invest Dermatol*. 2016;136(7):1382-1386. <https://doi.org/10.1016/j.jid.2016.02.804>
10. Sarac G, Ozcan KN, Baskiran A, et al. Dermatological signs in liver transplant recipients. *J Cosmet Dermatol*. 2021. jocd 13944. <https://doi.org/10.1111/jocd.13944>
11. Otley CC, Cherikh WS, Salasche SJ, McBride MA, Christenson LJ, Kauffman HM. Skin cancer in organ transplant recipients: effect of pretransplant end-organ disease. *J Am Acad Dermatol*. 2005;53(5):783-790. <https://doi.org/10.1016/j.jaad.2005.07.061>
12. Ashraf T, Faisal N, Sonika G, Jafri SM. S1061 skin cancer screening and incidence in African Americans following liver transplantation. *Am J Gastroenterol*. 2020;115:S538. <https://doi.org/10.14309/01.ajg.0000706292.83932.96>
13. Ge L, Chee SN, Robledo KP, Lowe P. Comparison of skin cancers in liver and renal transplant recipients: results of a prospective study in an Australian tertiary referral centre. *Australas J Dermatol*. 2018;59(4):291-296. <https://doi.org/10.1111/ajd.12759>
14. Sng J, Koh D, Siong WC, Choo TB. Skin cancer trends among Asians living in Singapore from 1968 to 2006. *J Am Acad Dermatol*. 2009;61(3):426-432. <https://doi.org/10.1016/j.jaad.2009.03.031>
15. Oh CC, Lee HY, Tan BK, Assam PN, Kee TYS, Pang SM. Dermatological conditions seen in renal transplant recipients in a Singapore tertiary hospital. *Singapore Med J*. 2018;59(10):519-523. <https://doi.org/10.11622/smedj.2018126>
16. Chin-Hong PV, Reid GE, AST Infectious Diseases Community of Practice. Human papillomavirus infection in solid organ transplant recipients: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;33(9):e13590. <https://doi.org/10.1111/ctr.13590>
17. Schmook T, Nindl I, Ulrich C, Meyer T, Sterry W, Stockfleth E. Viral warts in organ transplant recipients: new aspects in therapy. *Br J Dermatol*. 2003;149(suppl 66):20-24. <https://doi.org/10.1046/j.0366-077x.2003.05627.x>
18. Snast I, Kaftory R, Lapidoth M, et al. Combined pulsed dye laser and systemic retinoids for the treatment of hypertrophic resistant warts among organ transplant patients. *Lasers Med Sci*. 2020;35(7):1653-1657. <https://doi.org/10.1007/s10103-020-03011-4>
19. Leow MQH, Oon HHB. The impact of viral warts on the quality of life of patients. *Dermatol Nurs*. 2016;15(4):44-48.
20. Forman D, de Martel C, Lacey CJ, et al. Global burden of human papillomavirus and related diseases. *Vaccine*. 2012;30(suppl 5):F12-F23. <https://doi.org/10.1016/j.vaccine.2012.07.055>
21. Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S. Human papillomavirus and cervical cancer. *Lancet*. 2007;370(9590):890-907.
22. Chahoud J, Semaan A, Chen Y, et al. Association between  $\beta$ -genus human papillomavirus and cutaneous squamous cell carcinoma in immunocompetent individuals—a meta-analysis. *JAMA Dermatol*. 2016;152(12):1354-1364. <https://doi.org/10.1001/jamadermatol.2015.4530>
23. Howley PM, Pfister HJ. Beta genus papillomaviruses and skin cancer. *Virology*. 2015;479-480:290-296. <https://doi.org/10.1016/j.virol.2015.02.004>
24. Wang J, Aldabagh B, Yu J, Arron ST. Role of human papillomavirus in cutaneous squamous cell carcinoma: a meta-analysis. *J Am Acad Dermatol*. 2014;70(4):621-629. <https://doi.org/10.1016/j.jaad.2014.01.857>
25. Quint KD, Genders RE, de Koning MN, et al. Human beta-papillomavirus infection and keratinocyte carcinomas. *J Pathol*. 2015;235(2):342-354. <https://doi.org/10.1002/path.4425>
26. Harwood CA, Toland AE, Proby CM, et al. The pathogenesis of cutaneous squamous cell carcinoma in organ transplant recipients. *Br J Dermatol*. 2017;177(5):1217-1224. <https://doi.org/10.1111/bjd.15956>
27. Sterling JC, Gibbs S, Haque Hussain SS, Mohd Mustapa MF, Handfield-Jones SE. British Association of Dermatologists'



- guidelines for the management of cutaneous warts 2014. *Br J Dermatol.* 2014;171(4):696-712. <https://doi.org/10.1111/bjd.13310>
28. Pham CT, Juhasz M, Sung CT, Mesinkovska NA. The human papillomavirus vaccine as a treatment for human papillomavirus-related dysplastic and neoplastic conditions: a literature review. *J Am Acad Dermatol.* 2020;82(1):202-212. <https://doi.org/10.1016/j.jaad.2019.04.067>
  29. Nichols AJ, Gonzalez A, Clark ES, et al. Combined systemic and intratumoral administration of human papillomavirus vaccine to treat multiple cutaneous basaloid squamous cell carcinomas. *JAMA Dermatol.* 2018;154(8):927-930. <https://doi.org/10.1001/jamadermatol.2018.1748>
  30. Otley CC, Griffin MD, Charlton MR, et al. Reduction of immunosuppression for transplant-associated skin cancer: thresholds and risks. *Br J Dermatol.* 2007;157(6):1183-1188. <https://doi.org/10.1111/j.1365-2133.2007.08203.x>
  31. Brennan DC, Aguado JM, Potena L, et al. Effect of maintenance immunosuppressive drugs on virus pathobiology: evidence and potential mechanisms. *Rev Med Virol.* 2013;23(2):97-125. <https://doi.org/10.1002/rmv.1733>
  32. Dharancy S, Catteau B, Mortier L, et al. Conversion to sirolimus: a useful strategy for recalcitrant cutaneous viral warts in liver transplant recipient. *Liver Transpl.* 2006;12(12):1883-1887. <https://doi.org/10.1002/lt.20927>
  33. Bonatti H, Aigner F, De Clercq E, et al. Local administration of cidofovir for human papilloma virus associated skin lesions in transplant recipients. *Transpl Int.* 2007;20(3):238-246. <https://doi.org/10.1111/j.1432-2277.2006.00430.x>
  34. Dantal J, Hourmant M, Cantarovich D, et al. Effect of long-term immunosuppression in kidney-graft recipients on cancer incidence: randomised comparison of two cyclosporin regimens. *Lancet.* 1998;351(9103):623-628. [https://doi.org/10.1016/S0140-6736\(97\)08496-1](https://doi.org/10.1016/S0140-6736(97)08496-1)