

## PAPAYYA THERAPY FOR CHRONIC ULCER: A RETROSPECTIVE COHORT AND META-ANALYSIS

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**ABSTRACT: SUMMARY BACKGROUND/OBJECTIVE:** Papayya wound therapy (PWT) has been used in various wounds including diabetic foot ulcers, venous leg ulcers, pressure ulcers, and acute surgical wounds. However, the efficiency of PWT therapy has been controversial. We therefore conducted a cohort study and a meta-analysis to assess PWT effects. **METHODS:** A retrospective cohort study was performed in diabetic foot ulcer (DFU) patients who were treated with PWT or conventional wound therapy (CWT) in Mahatma Gandhi Memorial Hospital Warangal Telangana State India. The Kaplan-Meier curve was applied to estimate the healing probability. A meta-analysis was performed to pool our study with four previous cohort studies identified from Medline and Scopus. **RESULTS:** The estimated incidence of wound healing was 5.7/100 (95% CI: 4.49, 7.32) patients-week, and the median time to healing was 14 weeks. The hazard ratio (HR) of wound healing was 7.87 times significantly higher in the PWT than the CWT ( $p < 0.001$ ) after adjusting for duration and size of ulcers, ankle brachial index (ABI), and glycated haemoglobin (HbA1c). Meta-analysis was applied and suggested that the treatment effects were moderately heterogeneous {Chi-square  $Z$  6.18 [degrees of freedom (d. f.)  $Z$  4];  $p$   $Z$  0.186;  $I^2$   $Z$  35.2%}, with the pooled risk ratio (RR) of 1.77 [95% confidence intervals (CI)  $Z$  1.01, 3.11], i.e., the chance of wound healing was 20% significantly higher with PWT than CWT. The average costs of department of Surgery, Mahatma Gandhi Memorial Hospital Warangal Telangana State India. **KEYWORDS:** Chronic ulcer, Chronic wound, Papaya, Papayya wound therapy; Wound therapy.

### INTRODUCTION:

**BACKGROUND:** One of the important aspects of wound management, especially in intractable wounds, is removal of necrotic tissue, which is known as debridement. The use of papayas for this purpose has been claimed to be an efficacious method. That stimulates wound healing, reduces the bacterial load, and eradicates methicillin resistant *Staphylococcus aureus* in vitro. Papayya wound therapy (PWT) has been applied in various settings, e.g., diabetic foot ulcers (DFU), 8, 9 peripheral arterial diseases, 10 venous leg ulcers, 11 pressure ulcers, 12 and acute surgical wounds. 13, 14

The use of PWT is increasing as a reflection of the increasing acceptance. The recent enthusiasm for PWT is supported and calls for public attention. However, the results of PWT treatment are still controversial. 10 A randomized controlled trial (RCT) 15 could not demonstrate differences in the rate of wound healing and healing time between PWT and standard treatment in venous leg ulcers, although PWT did reduce the time to debridement by approximately 2 days, but with significantly higher pain scores. The cost-effectiveness of PWT has been reported in some studies with conflicting results PWT was initially shown to have lower costs of treatment and require fewer visits, but these could not be confirmed in a recent RCT study.

## ORIGINAL ARTICLE

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We, therefore, performed a retrospective cohort study and follow-up meta-analysis of comparative studies to evaluate wound healing outcomes with PWT compared with conventional wound therapy (CWT).

### **MATERIALS AND METHODS:**

**COHORTSTUDY:** A retrospective cohort study was performed by reviewing the medical records of diabetic DFU patients who were treated at Mahatma Gandhi Memorial Hospital Warangal Telangana State India a 1000 beds hospital from January 2013 to December 2013. Patients who met the following criteria were included in the study,<sup>(1)</sup> presence of a single wound of the foot,<sup>(2)</sup> ability to walk without the use of a wheelchair or other assistive device,<sup>(3)</sup> data were available for at-least 6 months of follow-up; and,<sup>(4)</sup> no gangrenous wounds, necrotizing fasciitis, abscess, or osteomyelitis present. Patients were assigned by surgeons who were well trained in chronic wound care, to receive PWT or CWT at the out-patient clinic or in-patient wards, based on surgeon's judgment.

Then, papayas cut into small pieces after peeling of the skin in aseptic way, was applied to the wounds, with an average of one papaya pieces/cm<sup>2</sup> of wound surface.<sup>(5)</sup> The wound was covered with wet light gauze, and the entire foot was loosely bandaged. The median number of applications of papayas was 8.25 [standard deviation (SD) 5.13] times/patient. For the control group, the wound was dressed with normal saline or hydrogel and debridement was performed as judged by the treating surgeon.<sup>(6)</sup> The wounds were debrided with a median of 8.79(SD 5.14) times/patient. The wound was evaluated once/week by surgeons and evaluated using digital photographic images. Patients were classified as having wound healing if their wounds had 95% complete epithelial covering in the absence of a scab, and the wounds were suitable for split skin grafting, flap coverage, or self-healing. Healing time was defined as the time from treatment initiation to wound healing. Patients were followed up from treatment initiation until the end of December 2013. The study was approved by the Institutional Review Board prior to conducting the study and all participants had given informed consent.

**Meta-Analysis:** Studies were identified using PubMed and Scopus search engines from January 1946 to September 15, 2011. The search strategy is described in Appendix 1.

**Inclusion Criteria:** Comparative studies of PWT and CWT were included in the review if they met with the following criteria: patients aged 18 years and compared wound healing rate or wound healing time between groups. The reference lists of all relevant studies were also reviewed. If studies were duplicated, the one with the most complete data was chosen. For studies which reported in sufficient data, the corresponding authors were contacted and invited to provide more information. Two attempts were made to contact

**Outcomes:** The outcomes of interest were the rate of wound healing and/or healing time.

**Data Extraction:** Two investigators (CW and NP) independently extracted the data using a standard data extraction form. Information extracted included general data (author, year of publication, journal), study characteristics (study design, setting), patient characteristics at baseline (Age, type of wound, underlying disease, white blood cell count, ABI, percent amputation), and the outcomes as described above. Any disagreement was discussed and resolved by consensus with a third party (AT).

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