

Novel methods of wound closure - a systematic review

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ABSTRACT

Introduction: The primary goal of wound closure is the post-operative rapid closure to reduce the side effects such as bleeding time, pain, infections, cost, and management. **Objective:** Approximation of injured tissues after surgery is essential to restore their structure and enhance their function. Techniques and materials used for wound closure should be biocompatible, easy to apply, microbial resistance, less time-consuming, biodegradable, and inexpensive. **Search Strategy:** We searched PUBMED central for related topics from 2013 to July 2017. **Selection Criteria:** All the studies and articles that inferred the latest and most natural sources of wound closure after third molar extraction with less side effects as to conventional wound closure techniques were included. **Data Collection and Analysis:** All the studies included were based on the data extraction and analysis of the studies for quality and publication bias. The data collection form was customized. The primary outcome measures were on the effect of the novel techniques of wound closure on injury, infection, risk factors, and post-operative stability. **Main Result:** The reviews found some clinical evidence that there is a significant difference between the different novel techniques of wound closure with respect to injury, infection, risk factors, cost, and time, and post-operative stability. **Conclusion:** The clinical evidence in this review is adequate to state that there is an appreciable difference in the post-operative stability between the different novel techniques of wound closure but also highlights the challenges and problems which a clinician may encounter while using these various novel techniques which otherwise would not cause any problem if using the conventional suturing technique.

KEY WORDS: Cost-effective, Extraction, Infection, Stability, Suture, Time-consuming, Wound closure

BACKGROUND

Ideally, a wound closure method should be cost-effective, time-efficient, and easy to perform and produce the optimal cosmetic result. The primary goals of treating wounds in general and skin incisions, in particular, are rapid closure with an esthetic scar. Over the years, research on acute wound healing has resulted in the development of technologies such as staples and adhesives (e.g., glues and adhesive tapes) to allow surgeons to replace their complicated suturing techniques with simple, non-operator-dependent, safe resulting in minimal infections by immediately sealing the wounds using wide varieties of skin closure materials.^[1,2] As a result, many investigators have experimented with different materials, tissues, and models to close wounds, including laser-assisted tissue bonding.

Commercially available surgical materials are formed from natural or synthetic sources, or in a combination. Commonly used natural materials for surgical applications include fibrin, collagen, gelatin, and polysaccharides. Cyanoacrylates, various dendrimers, polyurethanes, and poly (ethylene glycol) (PEG) are examples of synthetic surgical materials.^[3] Various composite surgical materials have been also formed using both natural and synthetic polymers such as gelatin-resorcinol-formaldehyde albumin/PEG (Progel, Bard Inc.) dextran/(2-hydroxyethyl methacrylate), chitosan/polylysine, and PEG/dextran.^[4]

Suture knots present several disadvantages in wound closure because they are tedious to tie and can physically damage the normal tissue. Bulky knots may be a reservoir for infection, and they may transmit through skin weeks after surgery.^[5] Needle manipulations during knot-tying predispose the surgeon to glove perforation. A barbed suture was developed that is self-anchoring, requiring no knots

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Website: jprsolutions.info

ISSN: 0974-6943

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Received on: 18-05-2018; Revised on: 23-06-2018; Accepted on: 26-07-2018

for wound closure. The elimination of knot tying may have advantages over conventional wound closure methods.^[1] We introduced a simple technique using knotless, absorbable barbed suture material for wound closure.^[6]

Suturing is necessary during the extraction impacted mandibular third molars and is aimed at recovering the soft tissues for better healing. Furthermore, suturing reduces post-operative bleeding and narrows the extraction socket, which can prevent food from entering into it and protect the blood clots.^[7] The wound should not be sutured too firmly.

Actually, food more easily gets into the mandibular extraction wound under gravity, compared with the maxillary wounds. Thus, food impaction is a serious clinical problem after the mandibular impacted third molar extraction, except for pain, trismus, dry socket, and other common post-operative complaints. In a study, the molars were horizontally/mesioangularly impacted on both sides, and all teeth were partially or completely covered by mucosa.

- The region, size, and resistance distribution of the bilaterally impacted molars were similar.
- The patients were in good medical condition, without local inflammation.
- All patients were treated with the traditional method on one side and the new technique on the other side.
- All patients had complete medical records and follow-up records, and they could clearly remember the relevant complications after the tooth extraction.

This is a double-blind study with the patients have no knowledge at which site is which.^[5]

Aim

The aim of the study was to review various unconventional techniques for operative wound closures in oral maxillofacial surgery.

Structured Question

Which is the best method for wound closure taking into account, time consumption, infection risk, cosmetic scar, and cost-effectiveness?

PICO Analysis

Population

Patients undergoing treatment for mandibular or maxillary molar extraction were selected.

Intervention

Novel techniques of wound closure:

- Natural sources
- Synthetic sources
- Barbed suture
- Advanced technology.

Comparison

Assessment of healing of mandibular or maxillary teeth extraction sockets using different novel methods of wound closure.

Outcome

The outcomes are time-efficient, cost-efficient, minimal infection risk, and post-operative stability.

Null Hypothesis

There is no difference between the different novel techniques.

MATERIALS AND METHODS

Sources Used

For identification of studies considered for this review, detailed search information was developed for the database that was searched. The PubMed search used the combination of controlled vocabulary and free texts terms.

Searched Database

PUBMED (from 2013 to July 2017)

Search engine articles.

Language

Articles in English were only included.

Hand Search

The following journals were hand searched:

- Oral surgery oral medicine oral pathology
- International journal of oral and maxillofacial surgery
- British journal of oral and maxillofacial surgery.

Search Methodology

| Recent queries in PubMed | Query | Items found | Time |
|--------------------------|---|-------------|----------|
| #30 | Search (Pomegranate fruit extract) and wound closure Filters: Free full text | 0 | 08:46:22 |
| #31 | Search (Pomegranate fruit extract) and wound closure Schema: all Filters: Free full text | 0 | 08:46:22 |
| #29 | Search surgical materials Filters: Free full text | 24937 | 08:45:34 |
| #28 | Search absorbable suture filters: Free full text | 533 | 08:44:54 |
| #27 | Search evulsion filters: Free full text | 16 | 08:43:29 |
| #26 | Search (nanoparticles) and wound closure schema: All filters: Free full text | 0 | 08:41:37 |

| | | | |
|-----|---|-------|----------|
| #25 | Search (nano particles) and wound CLOSURE filters: Free full text | 0 | 08:41:37 |
| #6 | Search Babes suture and extraction Filters: Free full text | 0 | 08:39:32 |
| #24 | Search wound closure filters: Free full text | 4333 | 08:38:54 |
| #23 | Search Suture filters: Free full text | 10861 | 08:38:32 |
| #22 | Search (Laser) and wound closure filters: Free full text | 99 | 08:37:19 |
| #21 | Search (honey) and wound closure filters: Free full text | 7 | 08:36:43 |
| #20 | Search (Aloe vera) and Wound closure Filters: Free full text | 2 | 08:35:59 |
| #19 | Search (herbal materials) and wound closure filters: Free full text | 3 | 08:34:16 |
| #18 | Search (new methods) and extraction filters: Free full text | 3661 | 08:32:46 |
| #17 | Search (novel techniques) and extraction filters: Free full text | 1848 | 08:32:22 |
| #16 | Search novel techniques of wound closure Filters: Free full text | 160 | 08:30:55 |
| #14 | Search barbed suture Filters: Free full text | 95 | 00:36:55 |
| #13 | Search extraction and barbed suture Filters: Free full text | 1 | 00:06:44 |
| #12 | Search extraction filters: Free full text | 45890 | 00:06:29 |
| #10 | Search barbed suture and extraction filters: Free full text | 1 | 00:05:59 |
| #11 | Search barbed suture and extraction filters: Free full text | 1 | 00:05:09 |
| #9 | Search anesthesia filters: Free full text | 1 | 00:02:38 |
| #8 | Search Barbed suture and wound closure filters: Free full text | 242 | 00:02:38 |
| #4 | Search wound closure and extraction Filters: Free full text | | |

Inclusion Criteria

The criteria for considering studies for this review are as follows:

Types of studies:

1. Randomized controlled trials or clinical trials.
2. Incorporating the different novel techniques of wound closure were considered [Table 1].

Types of participants:

- Patients with mandibular or maxillary extractions.

Types of interventions:

- Natural sources, synthetic sources, barbed suture,

and advanced technology.

Types of outcome measures:

- Time-efficiency, cost-efficiency, minimal infection risk, and post-operative stability involved in the different novel techniques of wound closure.

Exclusion Criteria

The following criteria were excluded from the study:

1. Case reports
2. Studies not containing statistical analysis
3. Studies with an insufficient sample size of <10 in the group.

RESULTS

Description of Studies

The search identifies 20 publications out of which 5 were excluded after reviewing the title or abstract. Full articles were obtained for 15 studies, 10 of these publications were excluded after reading the full text articles [Table 2]. Therefore, a total number of five publications fulfilled all the criteria for inclusions [Flow chart 1].

Quality Assessment

The quality assessment of included trials was undertaken independently as a part of data extraction process. Three main criteria were examined:

1. Method of randomization, recorded as
 - A. Yes - adequate
 - B. No - inadequate
 - C. Unclear
2. Allocation concealment, recorded as
 - A. Yes - Adequate
 - B. No - inadequate
 - C. Unclear
3. Completeness of follow-up assessed as:
 - A. Yes - dropouts were explained
 - B. No - dropouts were not explained
 - C. None - no dropouts or withdrawals

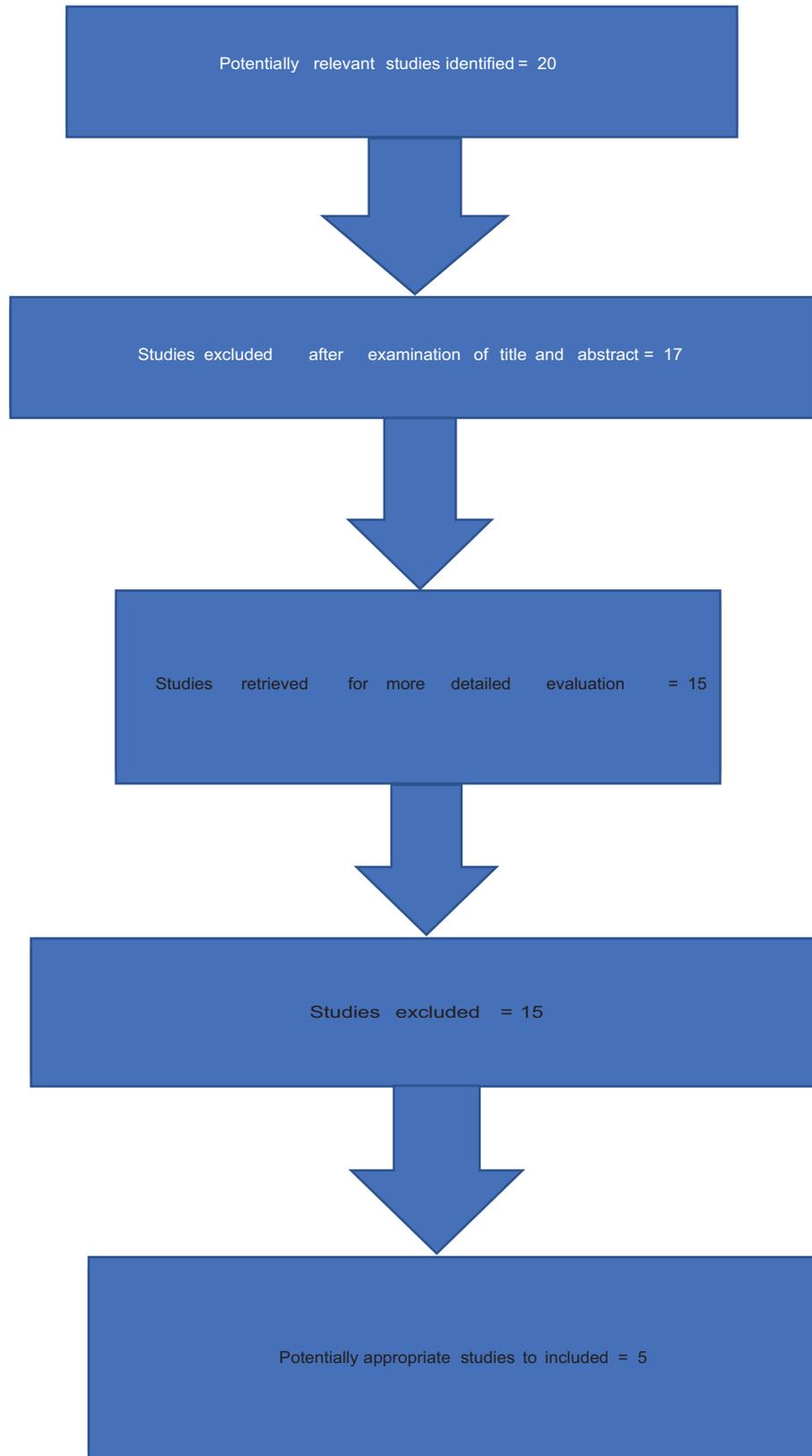
DISCUSSION

Suture

Egyptian scrolls going to as early as 3500 bc depicted wound Closure utilizing suture material. In the past, there has been a significant number of suture

Table 1: Variables of interest

| |
|--------------------------|
| Variables of interest |
| Post-operative stability |
| Injury |
| Infection |
| Cost-effective |
| Time efficient |
| Risk factors |



Flow chart 1: Search criterion

Table 2: Characteristics of excluded studies

| Author | Year | Reason for exclusion |
|---------------------------|------|--|
| Vujanovic and Vujanovic | 2013 | No radiograph evolution |
| Annabi <i>et al.</i> | 2017 | No comparison group |
| Sharma <i>et al.</i> | 2013 | No comparison group, insufficient parameters |
| Tarameshloo <i>et al.</i> | 2009 | Comparison groups are not relevant |
| Boudreau and Beland | 2006 | Insufficient cases |
| Annabi <i>et al.</i> | 2014 | Small sample size |

Table 3: General information of selected articles

| Author | Year | Country | Sample size | Study design | Age | Set up | Method of evaluation |
|----------------------------|------|-----------|-------------|----------------------------|-------|------------|---------------------------------------|
| Al-Mubarak and Al-Haddab M | 2014 | Pakistan | 56 | Randomized clinical trials | 18–45 | College | Clinical evaluation |
| LaBagnara | 2000 | France | 75 | Randomized clinical trials | 25-30 | University | Clinical evaluation and radio graphic |
| Kim | 2016 | Japan | 50 | Randomized clinical trials | 40–45 | College | Clinical evaluation |
| Kwakman and Zaat | 2012 | Argentina | 92 | Randomized clinical trials | 30–40 | College | Clinical evaluation |
| Sterling and Skouge | 2008 | England | 50 | Randomized clinical trials | 30–40 | University | Clinical evaluation |

Table 4: Results

| Author and year | Materials used | Method of evaluation | Parameters and values | Outcome |
|--------------------------------|-------------------------------|--|--------------------------------------|--|
| Al-Mubarak and Al-Haddab, 2014 | Staples, barbed suture, laser | Clinical evaluation | Stability (13.4%) injury (16%) | Significant difference between the three techniques, but laser caused more complications |
| LaBagnara 2000 | Fibrin and collagen-based | Clinical evaluation, radiographic evaluation | Stability (14.3%) infection (10%) | Significant, highlights the complications of fibrin and collagen-based |
| Kim, 2016 | Barbed suture | Clinical evaluation | Stability (23.4%) injury (4%) | Significant |
| Kwakman and Zaat, 2012 | Honey, pomegranate | Clinical evaluation | Stability (20%) injury (1%) | Significant difference is present suggesting; honey is better |
| Sterling and Skouge, 2008 | Laser | Clinical evaluation | Stability (76%) injury | Significant |

materials, including animal tendons, horsehair, vegetable fibers, and human hair.^[4] Over 1806, Philip Syng Physick created an absorbable suture with buckskin.^[4] Basically inventing the present day procedure of suturing. To successfully repair the skin, it should induce no foreign body reaction, smooth surface and not difficult to handle. In addition, it should secure the knots and insert minimal trauma. Suture strength, infection risk, tissue-holding power, and incision-type need to be considered [Tables 3 and 4]. To choose the right procedure, it is based on the physical and biological properties of suture material, suturing technique, and the healing properties of the sutured tissues.^[5,6]

Anesthesia Method

All patients received one-time block anesthesia in the inferior alveolar nerve, lingual nerve, and buccal nerve using a 2% lidocaine hydrochloride (1:200,000 epinephrine) anesthetic solution. Terminal infiltration of the buccal fold and distal incision region was also performed using primacaine with adrenaline.

Natural Sources

Natural source-based sutures are derived from human blood and natural polymers such as collagen and gelatin. Fibrin-based surgical materials are one of the most commonly used glues in clinical applications. They are made from two main components, fibrinogen and thrombin, with a small quantity of calcium chloride to form surgical materials which have two applications; hemostat and sealant. The fibrin is polymerized from the fibrinogen, and then a white fibrin clot is generated with thrombin and CaCl_2 . Commercially available examples are Crosseal and Heamseal APR. Even though they have advantages, such as biocompatibility and fast curing, some disadvantages are also seen, including poor adhesion and mechanical strength [Tables 3 and 4].

Collagen-based surgical materials are biocompatible and have low risk of transmission compared to fibrin. The most commonly used collagen-based surgical materials are processed; its composition contains bovine collagen and bovine thrombin, and CoStasis, which is

made of human plasma, bovine collagen, and thrombin. Similar to fibrin, collagen-based adhesives have low adhesion and mechanical strength [Tables 3 and 4].

Aloe vera is also called as aloe barbadensis. It is a cactus-like plant, present in tropical areas belonging to the Liliaceae family. Two products are derived from after processing this plant; the Aloe vera latex and the Aloe vera gel.

These products were approved by the US food and drug administration as a laxative and cathartic agent.^[7-9] It contains several biologically active compounds, such as soluble sugars, non-starch polysaccharides, lignin, lipids, Vitamins (B₁, B₆, and C), salicylic acids, proteins, and minerals (sodium, calcium, magnesium, and potassium). Its various functions include anti-inflammatory (due to the presence of glycoproteins, like lectins), antiseptic, and antimicrobial properties.^[10] The AV gel also retains the ability to stimulate fibroblast proliferation, collagen synthesis, and angiogenesis (due to the presence of acemannan, peptic acid, etc.).

A randomized controlled clinical trial that investigates the effects of Aloe vera gel on the healing process of sutured incision wounds in rats showed that AV gel significantly increases the fibroblast proliferation, angiogenesis, re-epithelialization, and wound closure. These effects can be due to the improved infiltration of AV within the skin tissue, which stimulates the biological activities involved in the wound healing throughout the repair process.^[11]

Khorasani *et al.*^[7] conducted a randomized clinical trial to investigate the efficacy of AV cream (0.5% of AV gel powder) in second-degree burn wounds. The study involved 30 patients with similar burn wounds at two different sites in the body. One wound was treated with Aloe vera and the other was treated with SSD. The ones treated with Aloe vera showed faster re-epithelialization and less time to heal.

Honey

It is viscous, concentrated acidic sugar solution with a pH of four produced by honeybee *Apis mellifera*. Its chemical composition includes carbohydrates such as fructose (40%), glucose (30%), and sucrose (5%), water (20%), amino acids (5%), antioxidants, vitamins, minerals, and enzymes.^[12] It has various functions such as antibacterial, anti-inflammatory, antifungal, and the ability to stimulate angiogenesis, granulation, wound contraction, and epithelialization. *In vitro* studies also showed that honey promotes the angiogenesis in a rat aortic ring assay^[13] and stimulates the proliferation of human keratinocyte cells, which are involved in the healing process and play a primary role in re-epithelialization. Majtan *et al.* showed that either honey solution or Major Royal Jelly Protein 1 (MRJP1)

induces the proliferation of human keratinocytes.^[14] Honey increases the expression of cytokines and matrix metalloproteinases-9 mRNA in primary keratinocytes, which, in turn, increases MRJP1 expression, leading to increased wound healing [Tables 3 and 4].

Pomegranate

Fruit extract is the latest source used for post tooth extraction wound healing. Has several activities such as anti-inflammatory, antibacterial, and stimulation of vascular endothelial growth factor (VEGF), and PDGF pathways. The two main antioxidants are present in punicalagin and ellagic acid. In a study, 12 cavia cobaya^[15] was taken and divided into two groups, one containing sodium carboxymethylcellulose and the other with pomegranate extract. The lower jaw of experimental animals was taken, decalcified for 30 days. Moreover, the VEGF and platelet-derived growth factor (PDGF) activity on the 4th day of wound healing was tested using immunohistochemical techniques. In this research, the increased VEGF expression was accompanied with the increased PDGF expression. The number VEGF and PDGF expression by macrophages^[16] and fibroblasts were less in the control group compared to the treatment group using *t*-test ($P < 0.005$). So decreased expression of PDGF leads to reduced wound healing [Tables 3 and 4].

Barbed Suture

Introducing a simple technique using knotless, absorbable barbed suture material has had significant improvement in successful wound closure. In a study conducted using consecutive 31 patients (22 males), divided into two groups, one control with conventional suturing and one treated underwent uniportal video-assisted thoracoscopic surgery along with barbed suture for pneumothorax. There was slight difference between both groups ($P = 0.006$) with less operation time and less complications.^[17] In a study Sah compared barbed to traditional interrupted sutures in 50 TKA patients. The author noted that the barbed suture led to a mean faster closure time of 4.7 min ($P < 0.001$). Although the material cost was higher in the barbed suture cohort compared to the interrupted group (82 vs. 32 USD), the barbed sutures still led to greater savings by minimizing hospital stay and post-operative complications [Tables 3 and 4].

Advance Technology

The use of wavelength-specific dye-absorbers such as indocyanine green (ICG) and adhesive proteins such as albumin to laser may lead to faster and stronger close up of tissues than the traditional suture techniques. The presence of water content and absorption capability in the body is the main aspect for laser. Holmium: YAG and CO₂ were used initially, but causes unwanted excess heat production which causes irreversible

tissue damage [Tables 3 and 4]. ICG is the best laser technique to use along with albumin diode. Because it can be done under temperature controlled system and using diode helps in High absorption of water in the near-infrared region. subdivided into two main sub-phases: photochemical tissue bonding (PTB) and photothermal tissue bonding. Kirsch *et al.*^[18] used laser tissue soldering through a low-power laser to repair hypospadias, to decrease complications of conventional suturing techniques. It is performed in almost in suture less fashion. Many animal studies have shown that with fewer sutures, reduces inflammatory responses. Simhon *et al.*, with porcine models^[19], suggested that the scars resulted from suturing are thicker compared to laser-induced wound closure.

Defending the Result

The novel techniques seen in the majority of trials seem to give post-operative stability and less infection risk, especially impacted third molars. However, the difference in stability is very less between different techniques, compared to the difference in infection, risk factors. Thus, our conclusion is the type of technique used should be according to post-operative stability. At the same time, since the studies did not show extremely significant differences, it is also suggested to carry out further studies involving a larger sample size and newer and more advanced laser techniques.

CONCLUSION

These findings suggest that the use of novel techniques either from natural sources or synthetic was efficacious enough to provide post-operative stability with minimal infections. The advanced laser technology is difficult to adapt and difficult to use in cases of sinus lift. However, the operation time is shorter and less material is needed in that region. Studies with a larger sample size are necessary to correlate with the findings of present study for their wider use in clinical practice.

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