Autoamputation of diabetic toe with dry gangrene: a myth or a fact?

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Abstract: Diabetes is associated with various complications and reduced quality of life. Of the many complications, some are life-threatening. Among these, foot complications remain an important concern. The major foot complications include foot ulceration, cellulitis, abscess, wet gangrene, dry gangrene, and necrotizing fasciitis, with different pathophysiological concepts behind each of them. Gangrene occurs due to reduced blood supply in the body tissues that leads to necrosis. This condition may arise because of an injury, infection, or other health conditions, majorly diabetes. Gangrene is classified as dry, wet, and gas gangrene. In case of wet and gas gangrene, surgical amputation is usually performed to prevent the spread of infection to other tissues. In dry gangrene, due to the presence of clear demarcation, autoamputation is preferred in certain parts of the globe. The present review aims to analyze the mode of dry gangrene management in diabetic patients based on previous evidence and plans to highlight various management strategies available for dry gangrene and the advantages/disadvantages of different treatments with special consideration to autoamputation.

Keywords: dry gangrene, amputation, surgical amputation, diabetic foot, diabetic toe, foot care.

Introduction
Diabetes occurs due to impairment in either pancreatic production of insulin or utilization of the produced insulin. It is one of the leading causes of deaths worldwide, the other causes being acquired immune deficiency syndrome, malaria, and tuberculosis. With time, the worldwide prevalence of diabetes has increased more in the developing countries than in the developed ones. The global diabetes burden has increased from 4.7% in 1980 to 8.5% in 2014. The Gulf countries including Saudi Arabia, Kuwait, and Qatar, along with the North African countries have the second highest number of diabetics globally. With this trend, the number of diabetics in the Middle East and North African region is expected to increase by 96.2% in the next 17 years. The disease along with its associated complications has placed the Arab governments under a huge economic burden.

Diabetes is associated with various complications and reduced quality of life (QoL). Of the many complications, some are life-threatening. Among these, foot complications remain an important concern. The major foot complications include foot ulceration, cellulitis, abscess, wet gangrene, dry gangrene, and necrotizing fasciitis, with different pathophysiological concepts behind each of them. As per the World Health Organization, there are always higher chances of limb amputation among diabetic patients as compared to non-diabetics. Amputation may lead to longer hospital stay, increased
Gangrene: an overview
Gangrene occurs due to reduced blood supply in the body tissues that leads to necrosis. This condition may arise because of an injury, infection, or other health conditions, majorly diabetes. Gangrene is classified as dry, wet, and gas gangrene (Table 1).

Dry gangrene
Dry gangrene is a condition that involves tissue death and turns it dry, dark, and mummified due to arterial occlusion. It takes place gradually, progresses slowly, and affects the lower extremities of the body (toes and feet) due to insufficient blood supply to the tissues. Dry gangrene is very common in individuals suffering from arteriosclerosis, high cholesterol, diabetes, and smoking. As per the International Diabetes Federation global report in 2015, 9.1–26.1 million people with diabetes develop foot ulcers, which may further lead to gangrene. In dry gangrene, due to necrosis, the tissue becomes shrunken and blackened and gets detached. In this condition, autoamputation is usually practiced due to occurrence of clear lines of demarcation. If dry gangrene is left untreated or
Autoamputation in diabetic toe dry gangrene

Wet gangrene
Wet or moist gangrene is a condition that occurs due to compromised or immobile venous and/or arterial blood, which leads to bacterial infection or sepsis. It mainly affects the body tissues which are naturally moist (oral tissues, respiratory tissues, cervix, and vulva). Diabetics are always at a high risk of compromised skin integrity and impaired wound healing due to peripheral neuropathy, vascular insufficiency, and hyperglycemia. Thus, being infection prone, diabetic patients are very susceptible to wet gangrene condition. As wet gangrene spreads quickly and can be fatal, prompt treatment is preferred.11,13 In case of wet gangrene, surgical amputation is usually performed to prevent the spread of infection to other tissues.14

Gas gangrene
Gas gangrene is a life-threatening infection where presence of gas at the infection site turns the tissue pale, bronze to purplish-red with development of multiple hemorrhagic bullae. Gas gangrene occurs in various clinical settings and can be classified as posttraumatic, postoperative, and spontaneous types. Spontaneous type of gas gangrene occurs in patients with any underlying conditions, majorly diabetes mellitus. It is a quickly spreading condition which involves the production of gas due to bacterial infection caused by Clostridium perfringens. An early identification and therapy with radical amputation is the best treatment of choice.11,15

Factors contributing to diabetes and associated dry gangrene
There are various factors that contribute to the occurrence and high prevalence of dry gangrene in diabetic patients. The factors commonly causing dry gangrene in diabetics are mentioned below.

Lifestyle
With modernization, the Gulf countries are nowhere lagging in following urban lifestyle. High-calorie foods, relying on technology, and sedentary lifestyle have contributed to an increase in the numbers of diabetics and obese patients in the Middle Eastern world. Adapting to a healthy lifestyle is the best way to reduce the risk of gangrene occurrence among diabetics. This includes consuming healthy diet and practicing regular exercise.16

Age/gender
The prevalence of diabetes-associated foot complications is directly proportional to advancing age. As per a retrospective cohort study conducted by Al-Rubeaan et al, rates of foot ulcers were reported to increase with age, with higher rates found (4.2%) for males aged ≥75 years and females aged between 65 and 74 years (2.5%).17

Foot care and habits
Diabetic patients are always at a high risk of developing foot complications. Wearing tight shoes, walking barefoot, and poor control over diabetes give access to foot complications. Hence, proper foot care and managing daily habits are mandatory.18

Education
Lack of education is another major factor that contributes to diabetic foot complications. As per a survey study by Nemcová and Hlinková, educating people to control obesity and blood pressure, and on foot care has shown positive effects on disease.19 Another hospital-based, cross-sectional study conducted in Saudi Arabia by Odhayani et al showed

<table>
<thead>
<tr>
<th>Feature</th>
<th>Dry gangrene</th>
<th>Wet gangrene</th>
<th>Gas gangrene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Commonly limbs</td>
<td>More common in bowel</td>
<td>Limbs</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Arterial occlusion</td>
<td>More commonly venous obstruction</td>
<td>Gases produced by Clostridium bacteria</td>
</tr>
<tr>
<td>Macroscopy</td>
<td>Organ dry, shrunken, and black</td>
<td>Part moist, soft, swollen, rotten, and dark</td>
<td>Organ red, cold, pale, numb, shriveled up, and auto-amputation</td>
</tr>
<tr>
<td>Putrefaction</td>
<td>Limited due to very little blood supply</td>
<td>Marked due to congestion of organ with blood</td>
<td>Marked due to bacteria and infiltration of gases produced by them in tissues</td>
</tr>
<tr>
<td>Line of demarcation</td>
<td>Present at the junction between healthy and gangrenous parts</td>
<td>No clear-cut line of demarcation</td>
<td>No clear-cut line of demarcation</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Bacteria fail to survive</td>
<td>Numerous present</td>
<td>Major cause</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Generally better due to little septicemia</td>
<td>Generally poor due to profound toxemia</td>
<td>Generally poor due to quick spread to the surrounding tissues</td>
</tr>
</tbody>
</table>

Note: Data from NHP.gov.in.11

Table 1 Differences in features of dry gangrene, wet gangrene, and gas gangrene

The treatment is delayed, it may progress to cause infections and complicate the condition. Following autoamputation practice also increases the painful phase and decreases the QoL.9
that having little or no knowledge about the risk factors, future complications, and foot care in diabetes worsen the condition.20

Other factors that may contribute to diabetic dry gangrene include climate, weather conditions, and following various religious and cultural beliefs.21–23

**Pathophysiological factors in dry gangrene**

There are different pathways involved in the pathophysiology of dry gangrene (Figure 1). These include various metabolic, vascular, and neuropathy factors.24

**Metabolic factors**

Diabetes and obesity are the two main metabolic diseases. Hence, hemoglobin A1c and body mass index are directly proportional to the occurrence of gangrene condition. Poor glycemic control and obesity contribute to microvascular angiopathy and increased pressure on foot, respectively. Thus, these factors should be critically considered while treating gangrene patients. As per a prospective analytical study conducted by AlGoblan et al,25 early resolution of the foot ulcers occurred in 61% patients who were a normal weight, compared to 49% obese patients whose condition took more than double the time to resolve.26

**Vascular factors**

Vascular system plays an important role in the etiology of dry gangrene. Peripheral arterial disease/arteriosclerosis involves shrinking of the peripheral arteries, majority of which supply the lower extremities. It is mainly associated with ischemic claudication, which involves pain and cramps due to decreased blood supply to the tissues. Thus, the major culprit behind dry gangrene is ischemia. When chronic ischemia is worsened, it causes critical limb ischemia, which further results in discoloration, numbness, dryness, and necrosis of the affected part.11,27,28

**Neuropathy factors**

Patients with diabetic peripheral neuropathy are highly susceptible to foot complications, including gangrene and amputations. As per a large cohort study by Al-Rubeaan et al, diabetic patients usually face nerve compression in the lower limbs. Thus, examination and surgical decompression of the nerve should be considered. This helps in increasing the microcirculation as well as overall nerve function in the limbs.17

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**Figure 1** The pathophysiological pathways of dry gangrene

*Note: Adapted from: Rodrigues J, Mitra N.24*
Autoamputation in dry gangrene among diabetics

Autoamputation is the self-detachment of nonviable tissue from viable tissue. In dry gangrene, autoamputation is very commonly preferred, mainly in patients who are not good candidates for surgery. Due to nerve damage and reduced blood circulation to the extremities, foot ulcers and slow healing wounds occur, which further causes limb detachment. It is generally practiced for the distal portions of the affected limbs by leaving an intact tissue eschar. The risk of amputation in diabetes patients is around >25 times as compared to that in non-diabetics. The process of autoamputation may take several months and is a very uncomfortable phase. Thus, a long wait may make the condition worsen with increased pain and reduces the QoL in patients.9,29,30,31 Thus, an early diagnosis and treatment of dry gangrene should be considered very critical.

Management of dry gangrene

Before starting any treatment, it is important to diagnose the type and extent of gangrene. Diagnosis of gangrene starts with documentation of patient’s history, physical examination, blood tests, and other investigations. Information regarding chronic diseases, surgeries, smoking, and exposure to extremely cold conditions is needed for the diagnosis. Various tests and investigations can be carried out to confirm the diagnosis of gangrene. These include the following:

- Physical examination of the affected body part and blood tests to identify infection.
- Drainage sample collection or tissue culture is done to know the bacteria responsible for infection.
- Imaging tests such as X-ray, magnetic resonance imaging, and computerized tomography are performed to confirm the spread of gangrene and the extent of damage caused to the tissues. These scans also help in detecting the presence of blockages in blood vessels.32

Dry gangrene can very easily turn into wet gangrene causing wounds and related complications. Thus, the first step in treatment is to optimally manage wound care, especially those that originate from gangrene.33 Wounds associated with diabetic foot amputation are very critical, especially in patients with poor immunity.34 Hence, depending on the nature and type of wound, selection of an appropriate strategy for therapy depending on patient’s condition.35

Treatment of dry gangrene may be done through pharmacologic and nonpharmacologic strategies as appropriate.

Pharmacologic approach

Pharmacologic approach for the treatment of dry gangrene in diabetics involves management of different pathways that may worsen the patient’s condition (Table 2). This section elaborates the various strategies employed.36–38

Diabetes management

Poor glycemic control is one of the common factors responsible for causing or aggravating foot condition in diabetics. Thus, diabetes patients exhibit 15 times more chances of amputation than non-diabetics.39,40 Since diabetes is a metabolic disease, lifestyle changes positively impact patient’s health. Additionally, pharmacologic management is required with the intervention of antidiabetic agents. These drugs are selected depending on the patient’s condition, type/severity of diabetes, age, and other factors. Treatment of type 2 diabetes mellitus is recommended, either when glycemic control is not attained or when hemoglobin A1c increases to >6.5% in 2–3 months after incorporating lifestyle changes.41

A good glycemic control is required in diabetes patients to avoid future complications.39 Qari and Akbar reported in their retrospective study on Arabs that 59% of diabetes patients suffered from foot ulcers. Of these, 65% patients required debridement and 23.5% patients underwent limb amputation. Others had good glycemic control with oral hypoglycemic agents and insulin.40

Another retrospective cohort study by Schellhase et al demonstrated that a good glycemic control in type 2 diabetes patients decreases the chances of microvascular complications. This further prevents occurrence or aggravation of limb ulcers, gangrene, and amputations.42

Pain management

Gangrene is usually associated with intermittent claudication in the limbs of patients. Thus, it is important to effectively manage the pain to let patient continue exercises to improve circulation. Opioid analgesics are recommended for pain associated with chronic limb ischemia. Apart from vascular factors, neuropathic pain should also be managed as a priority.43

Circulation management

As the senile/dry gangrene is a consequence of ischemia, improving the blood circulation in limbs helps overcome peripheral artery disease.43 As per the American Diabetes Association, antiplatelet therapy or platelet aggregation...
inhibitors are highly recommended for preventing the vascular complications in diabetes patients. Apart from drugs, in dry gangrene patients with peripheral arterial disease, guideline-directed management and therapy should be followed to decrease arterial occlusion or impaired perfusion, prevent the progression of chronic critical limb ischemia, and improve the functional status of affected limbs. This involves exercises which are done under structured or unstructured programs. Structured exercise programs include intermittent walking followed by alternate rest time. These are organized in the health care facilities and are supervised by a trained health care professional. Unstructured home-based exercise programs also include walking as a major exercise without any supervisor’s guidance.

Massage therapy is also recommended to improve the circulation in limbs. Only light pressure massage is given to the affected limb to avoid any clot formation. Massage should be cautiously done in patients with stent, with special instructions given by the health care professional.

**Table 2 Pharmacologic approaches for gangrene management**

<table>
<thead>
<tr>
<th>Pharmacologic approach</th>
<th>Drugs class examples</th>
<th>Mechanism of action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain management</td>
<td>Opioids and opioid-like analgesics</td>
<td>Mimic the actions of endogenous opioid peptides by interacting with mu, delta, or kappa opioid receptors</td>
</tr>
<tr>
<td></td>
<td>Morphine, oxycodone, dextromethorphan, tramadol, tapentadol, oxycodone, morphine, tapentadol, tramadol, oxycodone, morphine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Topical medications: capsaicin, lidocaine</td>
<td>Provide local action on the skin to relieve pain</td>
</tr>
<tr>
<td></td>
<td>Antiprostaglandin agents</td>
<td>Prevent the aggregation of platelets and fibrinogenesis</td>
</tr>
<tr>
<td></td>
<td>Anticoagulants: heparin, fondaparinux, danaparoid, bishydroxycoumarin, warfarin, acenocoumarol, phenindione</td>
<td>Cause activation of anticoagulant factors, direct inhibition of thrombin, inhibition of synthesis of blood coagulation factor precursors (zymogens), and activation of protein C</td>
</tr>
<tr>
<td></td>
<td>Fibrinolytic agents: streptokinase, urokinase, alteplase, reteplase, tenecteplase</td>
<td>Cause lysis of thrombi/clot to recanalize the occluded vessels</td>
</tr>
<tr>
<td>Circulation management</td>
<td>Antithrombotic agents: aspirin, clopidogrel, prasugrel, ticlopidine, dipyridamole, abciximab, epifibatide, tirol IB, ticagrelor, vorapaxar</td>
<td>Prevent platelet aggregation and fibrinogenesis</td>
</tr>
<tr>
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</tr>
<tr>
<td>Antibiotics</td>
<td>Penicillins: flucloxacillin</td>
<td>Inhibit bacterial cell wall synthesis by binding to specific penicillin-binding proteins located inside the bacterial cell wall</td>
</tr>
<tr>
<td></td>
<td>Fluoroquinones: ciprofloxacin</td>
<td>Inhibit topoisomerase II (DNA gyrase) and topoisomerase IV, which are required for bacterial DNA replication, transcription, repair, strand supercoiling repair, and recombination</td>
</tr>
<tr>
<td></td>
<td>Antiprotozoals: metronidazole</td>
<td>In reduced form, they covalently bind to DNA, disrupt its helix structure, inhibit bacterial nucleic acid synthesis, and cause bacterial cell death</td>
</tr>
<tr>
<td></td>
<td>Carbapenems: ertapenem, meropenem</td>
<td>Show bactericidal activity by inhibiting the bacterial cell wall synthesis</td>
</tr>
<tr>
<td></td>
<td>Glycopeptides: teicoplanin, vancomycin</td>
<td>Inhibit the bacterial cell wall synthesis and cause cell death</td>
</tr>
<tr>
<td></td>
<td>Tetracyclines: doxycycline</td>
<td>Reversibly bind to 30S ribosomal subunits and possibly to 50S subunits, block the binding of aminoacyl tRNA to mRNA, and inhibit bacterial protein synthesis</td>
</tr>
<tr>
<td></td>
<td>Lincosamides: clindamycin</td>
<td>Inhibit bacterial protein synthesis by binding to 50S ribosomal subunits of the bacteria</td>
</tr>
<tr>
<td></td>
<td>Oxazolidinones: linezolid</td>
<td>Selectively inhibit bacterial protein synthesis by binding to bacterial ribosomes and prevent the formation of a functional 70S initiation complex</td>
</tr>
</tbody>
</table>

**Notes:**
- Data taken from Tripathi, NHS.org, and Drugbank.ca.

**Lipid-lowering agents**

Dyslipidemia plays a major role in the progression of diabetic toe gangrene. Thus, diabetes patients should undergo a regular lipid profile check-up. In a descriptive case series study performed by Memon et al, 55.11% cases were reported to have abnormal lipid profile and 44.89% cases had lipid profile within the normal range. As per Wagner’s scale, the percentage of patients with superficial ulcers (Grade I), ulcer extension (Grade II), deep ulcer with abscess (Grade III), gangrene of one foot (Grade IV), and extensive gangrene foot (Grade V) was found to be 30.61%, 19.39%, 21.42%, 16.33%, and 12.25% respectively. Significant difference ($p=0.001$) was found in gangrenous diabetic foot, grade IV and grade V.

Along with making lifestyle changes, diabetes patients with dyslipidemia should also consume lipid-lowering agents. Usually, statins or 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitors are considered to lower the bad cholesterol or low-density lipoproteins. There are various statins, and they...
have been reported to show a dip in low-density lipoprotein profile by 20%–40%.48

Surgical procedures
In dry gangrene, people wait for autoamputation to happen, either due to cultural beliefs or just as an option/alternative to surgery.49 Before any surgical decision, dry gangrene patients should be examined and treated for peripheral vascular disease. This includes reperfusion in the affected extremity for quick healing of the area affected by gangrene.50 Vascular surgeons perform various vascular examinations which include angiogram, ankle–brachial index test, carotid duplex, computed tomography angiography/magnetic resonance angiography tests, and duplex ultrasound.51

Angiogram
Angiogram is a diagnostic as well as a therapeutic procedure that involves the use of X-rays to know about the obstruction in arteries. This helps the vascular surgeons to take decisions about treatment to be provided. Angioplasty and stenting are mainly used to open the blocked or narrow vessels.51

Ankle–brachial index test
This test helps in determining arterial blood circulation and blood pressure in the lower extremities.51

Carotid duplex test
This test is done to know the rate of blood flow through carotid arteries. It helps in exploring the presence of any plaques that may cause carotid artery disease.51

Computed tomography angiography and magnetic resonance angiography
These are the computerized imaging tests that are useful in studying in the blood vessels. These techniques help the vascular surgeons to know the severity of disease.51

Duplex ultrasound
Duplex ultrasound is used to assess the blood flow status in blood vessels. With this technique, vascular surgeons easily explore existence of any occlusion or clot and plan the treatment.51

Skin perfusion pressure (SPP) and skin vascular resistance
SPP and skin vascular resistance measurements also help in distinguishing the patients who require vascular reconstruction or major amputation and the patients who only require foot care or require minor amputation (Figure 2). A prospective, double-blinded study by Castronuovo et al concluded that in ~80% cases, SPP helps in diagnosing the critical limb

Figure 2 Management of dry gangrene.
Note: Adapted from: Rodrigues J, Mitta N.24
Abbreviations: SPP, skin perfusion pressure; SVR, skin vascular resistance.
ischemia accurately. Thus, the management of diabetic gangrene should be individualized, taking all these factors into consideration.

Shellac
Shellac, a natural agent, is used as a part of complementary and alternative medicine. This approach is practiced in Arabic-speaking countries and in people who refuse to undergo surgical amputation. Shellac helps by acting as a shield to protect the gangrene tissues from further infections. As per a randomized, controlled, pilot study conducted by Alzahrani et al, the rate of amputation was found to be lower (46.2%) in Shellac-treated type 2 diabetes mellitus patients than in 10% povidone-iodine-treated group (60%).

Nonpharmacologic approach
Education/foot care
Implementation of proper guidelines and educating people are essential to reduce the burden of diabetic foot complications. A quantitative research study conducted by John showed that 33% of diabetes patients had average knowledge, 1.66% had poor knowledge, and the rest had good knowledge about foot care. In Gulf countries, the knowledge about foot care in diabetics is lacking, especially in rural areas. Hence, educational programs should be regularly conducted in hospitals and other health care institutions to increase awareness among the Arabian population.

Apart from medicines, it is important to inculcate the basic foot care habits in people. Patients should be taught to take care of any wounds and cuts on their lower extremities, consequences of not wearing footwear and wearing ill-fitting shoes, precautions while cutting nails, using hot water, and use of moisturizers. Patients should also be educated about the outcomes of “no foot care”, self-examination, hygiene, and exercise.

Changing the footwear regularly also helps in healing the ulcers and reduces the frequency of recurrence of ulcers. As per a prospective observational study conducted by Saleem et al in Saudi Arabia, 79% patients who changed their footwear showed earlier healing than those who did not change their footwear. Use of medicated shoes is also beneficial.

Autoamputation in diabetic dry gangrene
As mentioned in the previous section, autoamputation is usually practiced either in ischemic, dry, and non-infected gangrene or in cases where surgery is not recommended. Dry gangrene always has a potential to become infected due to moisture absorption from the surroundings. Thus, waiting for autoamputation may lead to worsening of the condition. Also, a long wait enhances the duration of pain and discomfort and reduces the patient’s overall QoL.

Role of surgical amputation in dry gangrene
Due to chronic ischemia, the tissue becomes numb, dry, wrinkled, and dead. Thus, in case of necrotic tissues or dry gangrene, revascularization does not show any benefits. As per various reported cases, it has been observed that the surgical amputation is helpful in quick recovery and in reducing the discomfort and health complications associated with dry gangrene. After the surgical removal of gangrene foot or toe, a course of antibiotics while wound is healing (for quick healing without infections) should be considered important.

In a case series, an 82-year-old female patient preferred surgical amputation over autoamputation to achieve quick recovery. Later, the patient received physical therapy and could successfully walk with the help of prosthetic shoe. In another case of a male diabetic patient from this case series report, the toe with osteomyelitis and necrosis was surgically amputated. The patient successfully recovered and healed with a course of antibiotics. The same case series reported a case of a 45-year-old diabetic female patient with dry gangrene in toes, who was made to undergo transmetatarsal amputation. After surgery, the patient successfully healed and walked with a special shoe.

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Conclusion
In conclusion, proper education and management of patients who are at high risk of dry gangrene may reduce the total disease burden and associated complications in Arab countries. Although autoamputation is very commonly practiced over surgical amputation, in extreme cases, delay in management of the condition or a long wait for autoamputation may worsen the progression of dry gangrene and the QoL. On the other hand, surgical or elective amputation may relieve the patients in lesser time with lesser duration of painful phase and better outcomes. Surgical amputation also positively impacts the patient’s functional ambulation with lesser risk of further limb deterioration and improved survival rates. Hence, the concept of autoamputation should be individualized and practiced with caution.

Disclosure
The author reports no conflicts of interest in this work.

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