# UNIVERSITÀ DEGLI STUDI DI TORINO

**Predicting Severity of Pathological Scarring Due to Burn Injuries: a Clinical Decision Making Tool Using Bayesian Networks**

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**Abstract**

**Background.** It is important for clinicians to understand which are the clinical signs, the patient characteristics and the procedures that are related with the occurrence of hypertrophic burns scar in order to carry out a possible prognostic assessment.

**Objective**. Providing clinicians with an ease-to use tool for predicting the risk of pathological scar.

**Methods**. A total of 703 patients with 2440 anatomical burn sites who were admitted to the Department of Plastic and Reconstructive Surgery – Burn Center of Traumatological Hospital in Torino between January 1994 and May 2006 entered in the analysis. A Bayesian network model was implemented.

Results. The probability of developing a hypertrophic scar was evaluated on a number of scenarios. The error rate of the BN model was assessed internally and it was equal to 24.83%. While classical statistical method as logistic models can infer only which variable are related to the final outcome, the BN approach displays a set of relationships between the final outcome (scar type) and the explanatory covariates (age and gender's patients; BSA, FT-BSA, burn anatomical area and WHT; the burn treatment options such as advanced dressings, type of surgical approach, number of surgical procedures, type of skin graft, ECT.

**Conclusions**. A web-based interface to handle the Bayesian Network model was developed on the website www.pubchild.org [burns header]. Each clinician who registered to the website can submit its own data in order to get from the BN model the predicted probability of observing a pathological scar type.

**Keywords:** Bayesian networks; Hypertrophic scar; Interaction models; Prediction models; Web assisted decision making

## 1. Introduction

Burn injury is often a devastating event with long-term physical and psychosocial effects. All deep second and third degree burns in fact are at risk to develop hypertrophic scars which can severely undermine the quality of survival [1].

Burn scars, meanly if hypertrophic or keloid, are cosmetically disfiguring and force the scarred person to deal with an alteration in body appearance, cosmetic deformities, discomfort, psychological stress [2]. The exact mechanisms of normal and abnormal scar formation have long remained despite the extensive literature regarding wound healing. Recently researchers have begun to delineate the complex biochemical signaling pathways that regulate these processes [3-4].

At same way it is important for clinicians to understand which are the clinical signs, the patient characteristics and the procedures that are mainly related with the occurrence of pathological scarring to carry out a possible prognostic assessment of the scar [5]. That is in view of producing a quotation of pathological scar by means the initial data on characteristics of the burn and of the patient. In previous studies the key research issue has been to discover and review the risk factors for pathological burn scars [6] . In particular Deitch et al, reported that an important indicator of wound problems occurrence was the time required for the burn to heal [7], furthermore Baker RH evidenced that bacterial colonization could increase the incidence of hypertrophic scarring of burn wound [8], and a prospective study about 70 consecutive burn patients revealed that young age and black race are factors associated with pathological scarring [6]. Also anatomic sites like neck and upper limb are at higher risk than the abdomen and perineum of pathological scarring [6]. Other studies evidenced that hereditary factors and low triiodothyronine serum levels increased the individual susceptibility to hypertrophic scar formation or poor prognosis [9-10].

Nevertheless these studies do not provide to a physician a prognostic tool for prediction in a patient by means the initial data the likelihood to have a pathological scar. Following the maxim that prevention of

complications is preferable to treatment of an established problem [11], burn care specialists are in fact searching for methods to identify patients who might benefit from prophylactic programs.

The aim of the present study is to evaluate the factors associated with an increased risk for developing pathological burn scars, and to provide by means of a Bayesian Network (BN), a probabilistic reasoning tool which has been increasingly applied in the recent years as an ease-of-use prognostic instrument for risk prediction[12-13].

## 2. Materials and methods

### *2.1 Data Source*

#### *2.1.1 Training Sample*

From January 1994 at the Department of Plastic and Reconstructive Surgery – Burn Center of Trauma Hospital in Torino, a standard reporting form for collecting data referred to scar process has been used. Clinical histories were constructed for all burn patients by abstraction of details from the clinical notes made during their stay in hospital as inpatients, and the details recorded of returns for clinic attendances as outpatients or return as inpatients for corrective surgery. The cohort consists of 703 patients and 2440 anatomical burn sites. Particularly in this study cohort the scar type was defined on the basis of the morphologic classification described by Magliacani et al [11] and the scar evolution, calculated in days from the manifestation until its complete remission, was assessed according to the classification groups described by Muir [10].

#### *2.1.2 Validation Sample*

From May 15, 2006 to May 15, 2007 the Department of Plastic and Reconstructive Surgery–Burn Center in Torino continued to use a standard form for the collection of data regarding the scarring process. The present cohort was made up of 49 patients and included a total of 162 anatomic burn sites. All patients were enrolled into a surveillance program after the completion of the burn wound healing phase to control and/or treat the post-burn scarring as necessary.

*2.2 Statistical methods*

A BN is a graphical model for reasoning about an uncertain domain. BNs are graphical structures whose nodes represent variables and whose arcs represent direct dependencies between them. The only constraint on arcs is that the resulting graph has no cycle, thus the resulting network is known as a directed acyclic graph [14]. While the structure of the network captures qualitative relationships among variables, their strength of is quantified by conditional probability distribution associated with each node.

Methods involving automated learning from data can be implemented in order to select variables and establish their modalities, to build the graph structure and to assign conditional probability tables associated with each node. Roughly, the BN components can be determined through elicitation from experts or learned from data or using some combination of the previous ones strategies [15].

Automated methods for building the BN were implemented. A Bayesian search procedure based on the thick-thin approach was used for carrying out the structure learning of the relationships among variables and the Expectation-Maximization (EM) algorithm was chosen to estimate the required conditional probabilities [16]. The BN was implemented using GeNie [17] to develop the structure and Netica [18] for learning the probabilities and for performing the validation phase.

As well as many of the current software tools, these software environments required variables assume a finite number of states, both for building the structure of the BN and for carrying out parameter learning. Thus continuous variables were discretized on the basis of quartiles (Burn Surface Area [BSA] and Full Thickness-BSA FT-BSA) and tertiles (Age, Wound Healing Time [WHT] and Excision and Coverage Timing [ECT]). In table 1, the nodes of the BN along with their modalities were listed. A sensitivity analysis was carried out for the outcome node (normal scare vs. hypertrophic scare) in order to identifying the most influential variables. For categorical states, sensitivity is calculated as the degree of entropy reduction or mutual information, which measures how much uncertainty about a specific event is expected to decrease when a new finding is available [19], and the expected reduction of real variance.

Finally, an external validation using the validation sample was performed in order to evaluate the performance of the BN as prediction and classification tool.

## 3. **Results**

The univariable analysis of predictors of post-burn pathological scarring is given in the table 2.
The analysis demonstrates: as negative prognostic factors for pathological scarring *(i)* a WHT more than 6 weeks, *(ii)* an area of full thickness BSA more than 57% and *(iii)* a number of surgical procedures more than 4; as positive prognostic factors for pathological scarring *(i)* the etiology of burn by sun or by electrical tools, *(ii)* some anatomical areas such as the abdomen and perineum and *(iii)* the burn treatment with advanced dressings.
In Figure 1 the Bayesian network along with the conditional probability tables learned by the EM algorithm is depicted. In table 3, results of the sensitivity analysis are showed. Sensitivity analysis resulted in a list of variables ranked according to the capability to change the posterior probability of a targeted node they have when new evidence is entered. Mutual information and beliefs of variances values provide an indication of the relative sensitivity of each variable. The value in each cell refers to the rank of each variable with respect to the outcome node. Variables with greater values have also a greater impact in predicting the exit.
In table 4 the probability of developing a hypertrophic scar is evaluated on a number of scenarios. The probability of observing the evidence is also reported. The error rate evaluated on the validation sample was 24.83%.

### *3.1 Web- based interface for the BN model*

Systems based on Web-technologies have become increasingly important in the clinical setting to perform real-time processing and monitoring frequencies and causes of health hazards [20].

A web based interface to handle the above Bayesian Network model for predicting pathological scars has been developed on the website www.pubchild.org [burn header]. Each clinician who registered to the website can submit its own data in order to get from the BN model the predicted probability of observing a pathological scar type.

After registering to www.pubchild.org, users can enter into the Burns form section on the left menu. They have to set their evidence for each node; Agent, Etiology, Wound Healing Time, Type of surgical approach, Type of skin graft, Number of surgical procedures, ECT, Age, Surgical scar treatment are allowed to handle also Not Available (NA) evidence. The data from the user is sent over the Internet to the server. A first e-mail notification which summarizes data entered is sent to the user. Data entered is stored in a secured database maintained for studying purposes. The server web application is designed to handle incoming data and put them into each node of the BN model and update probability values of the Scar Type. Finally, a second e-mail containing the BN predicted outcome along with its probability value will be sent.

**Discussion**

In medicine Bayesian Network systems are used for aiding in prognosis decisional process: inferring the most probable outcome of an observed problem given a set of symptoms, patient history, physical signs and applied treatment. They are especially useful in clinical domain because they allow for building a probabilistic network of causal dependencies and can be used for diagnostic and prognostic inference [21]. In fact, when modeling human disease, the goal of researchers is to investigate causal connections, the relative strengths of those connections and how to infer them from real, noisy observations. These graphs play a key role in the decomposition of large probability distribution functions because they provide a visual representation of the sets of random variables that are relevant to each other.
While a multivariate regression infers only about which variable are related to final outcome, the BN approach displays a set of relationships between the final outcome (scar type), the demographic characteristics (age and gender), the clinical variables (BSA, FT-BSA, burn anatomical area and WHT) and the burn treatment options (advanced dressings, type of surgical approach, number of surgical procedures, type of skin graft, ECT).
The qualitative structure of the BN evidenced how pathological scarring is directly connected with several variables such as the type of surgical approach, the burn anatomical area, the time for burn healing and the age of the burn patient. Furthermore the WHT is related to full thickness BSA and to the burn etiology which in turn depends on gender and age of the burn patient.

The graph suggested that the final outcome is directly linked to the WHT. This finding is in agreement with previous published studies. Since 1983 Deitch et al [7] stated that the best predictor of the development of hypertrophic scar is the WHT, and Cubison et al [22], analyzing data on 337 children with scalds, suggested that the healing time has to be taken into account to decide the kind burn treatment , conservative or not. This further justifies attempts to speed up the healing process even by means expensive wound healing dressings.

This clinical variable in our model is related with three intermediate factors: FT-BSA, etiology and sex. Patient age appears to correlate well with the occurrence of pathological scar development [6]. Younger age is related to higher risk of developing keloid or hypertrophic scars, which may be because of the greater capacity of younger skin for collagen synthesis or grater skin tension in younger individuals. In fact normal wound healing is characterized by an optimum balance between deposition and lysis of collagen. The prognosis of older patients are better than in younger patient: this is derivable from the profile display.

As shown in table 4, young patients (profile 4), less than 15 years old, with burns on the neck and a FT-BSA greater than 57% have a probability of a abnormal scare of 69.9%. Instead patients older than 65 years, like in profile 6, with burns on the neck and a FT-BSA greater than 57% have probability of a abnormal scare of about 54%.

Finally, patients between 15-65 years with burns on upper limb with FT-BSA ranging from 38-57 (profile 8) have the probability of developing a pathological scare of about 99%, even if they are not frequently encountered (probability of evidence equal to 0.12%).

Thus the BN output can aid the physician to establish a prognostic probability acquiring some initial clinical sign. This information could be important for the communication with the patient in which informed, well-judged and not unaware message about his prognosis is often required.

In conclusion BNs could make it possible to easily integrate risk information into clinical practice by allowing physician both to evaluate the mutual relationships between the prognostic risk factors and therapeutic alternative approaches and to give an assessment of patient prognosis.

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**Table 1.** Description of the variables in the Bayesian network. Continuous variables were discretized on the basis of quartiles (BSA and FT BSA) and tertiles (Age, WHT and ECT).

| Variable description | Node Acronym | Variable type | States description |
|---|---|---|---|
| Gender | Gender | Discrete | Female, Male |
| Age | Age | Continuous | <15; 15-65; >65 |
| Burn surface area | BSA | Continuous | <23; 23-47; 47-72; >72 |
| Full thickness burn surface area | FT BSA | Continuous | <19; 19-38; 38-57; >57 |
| Aetiology | Aetiology | Discrete | Chemical; Contact; Electrical; Flame; Scalds; Pressure; Flash; Sunburns; Steam |
| Burnt area | Burnt area | Discrete | Abdomen; Lower limb; Upper limb; Neck; Perineum; Head; Chest |
| Burn treatment | Burn treatment | Discrete | Medical; Surgical |
| Number of surgical procedure | NO | Discrete | 0; 1; 2; 3; 4; 5; 6 |
| Type of surgical approach | TSA | Discrete | Alexander; Dermal abrasion; Flap; Excision; Excision and auto SG; Excision and xeno SG; Excision and allo SG |
| Type of skin graft | TSG | Discrete | 1:2; 1:4; 1:6; Sheet |
| Wound healing time | WHT | Continuous | 3 weeks; 3-6 weeks; > 6 weeks |
| Excision and coverage timing (from burn trauma to the first surgical procedure) | ECT | Continuous | < 5 days; 5-20 days; >20 days |
| Scar Type | Scar Type | Discrete | normotrophic; hypertrophic; hypertrophic with contracture; contracted; atrophic |

**Table 2.** Odds Ratio (OR) of pathological scar and95% confidence interval (CI95%) are displayed by demographic, clinical and treatment characteristics.

| | No-Pathological Scars | Pathological Scars | | | | OR (CI95%) |
|---|---|---|---|---|---|---|
| | normotrophic | hypertrophic | hypertrophic with contracture | contracted | atrophic | |
| Gender (Male) | 65(692) | 61(551) | 59 (227) | 60(53) | 75(3) | **1.24 (0.99;1.56)** |
| Age | 38(25 to 54) | 38(24 to 54) | 36(24 to 52) | 41(22 to 59) | 31(15 to 51) | 0.94(0.81;1.10) |
| Burn Surface Area (BSA) (%) | 18(10 to 35) | 20(10 to 35) | 30 (15 to 45) | 15(10 to 30) | 10(8 to 14) | 1.15(0.97;1.36) |
| Full Thickness BSA (%) | 8(0 to 20) | 10(4 to 20) | 20 (10 to 30) | 10(5 to 25) | 10(7 to 11) | **1.54(1.22; 1.94)** |
| Aetiology | | | | | | |
| Chemical | 2(22) | 3(21) | 1 (5) | 1(1) | 50(1) | 0.91(0.43; 1.95) |
| Contact | 2(18) | 1(10) | 2 (6) | 3(2) | 0(0) | 0.72(0.27; 1.91) |
| Electrical | 3(29) | 1(6) | 0 (0) | 1(1) | 0(0) | **0.17(0.06; 0.49)** |
| Flame | 64(620) | 67(561) | 76 262) | 58(43) | 0(0) | |
| Scalds | 14(140) | 15(125) | 5(18) | 19(14) | 0(0) | 0.80(0.59; 1.10) |
| Pressure | 0(0) | 0 3) | 1(2) | 0(0) | 0(0) | NA |
| Flash | 13(128) | 12(104) | 16(54) | 18(13) | 0(0) | 0.96(0.65; 1.41) |
| Sunburns | 1(10) | 0(2) | 0 (0) | 0(0) | 0(0) | **0.14(0.04; 0.58)** |
| Steam | 1(6) | 1(6) | 0 (0) | 0(0) | 50(1) | 0.84(0.20; 3.49) |
| Burnt area | | | | | | |
| Abdomen | 9(98) | 7(67) | 1(5) | 0(0) | 0(0) | **0.41(0.30; 0.58)** |
| Lower limb | 22(234) | 35(321) | 12(48) | 1(1) | 50(2) | 0.90(0.70; 1.16) |
| Upper limb | 28(301) | 34(308) | 48(185) | 44(39) | 25(1) | |
| Neck | 7(71) | 3(26) | 13(49) | 18(16) | 0(0) | 0.72(0.51;1.03) |
| Perineum | 5(50) | 3(24) | 1(3) | 0(0) | 0(0) | **0.30(0.19;0.50)** |
| Head | 19(199) | 7(61) | 5(20) | 10(9) | 25(1) | **0.26(0.19; 0.34)** |
| Chest | 10(105) | 11(98) | 19(75) | 26(23) | 0(0) | 1.05(0.80; 1.39) |
| Burn treatment | | | | | | |
| Medical | 64(678) | 37(336) | 17(65) | 28(25) | 50(2) | **0.25(0.20; 0.31)** |

| | | | | | | |
|---|---|---|---|---|---|---|
| Surgical | 380 (36) | 569 (63) | 320 (83) | 63 (72) | 2 (50) | 1.00 [Reference |
| Number of surgical procedures | | | | | | **2.10(1.73; 2.56)** |
| 0 | 67(677) | 39(336) | 18(65) | 32(25) | 50(2) | |
| **1** | 25(256) | 43(373) | 48(168) | 40(31) | 50(2) | |
| 2 | 4(44) | 12(99) | 19(67) | 17(13) | 0(0) | |
| 3 | 1(15) | 4(35) | 9(31) | 8(6) | 0(0) | |
| 4 | 0(5) | 1(12) | 3(10) | 3(2) | 0(0) | |
| 5 | 1(7) | 1(5) | 3(9) | 0(0) | 0(0) | |
| 6 | 0(3) | 0(0) | 1(3) | 0(0) | 0(0) | |
| Type of surgical approach | | | | | | |
| Alexander | 1(4) | 1(7) | 1(4) | 0(0) | 0(0) | 1.05(0.13; 8.83) |
| Dermal abrasion | 4(14) | 2(14) | 1(4) | 3(2) | 0(0) | 0.55(0.26; 1.16) |
| Flap | 2(6) | 0(0) | 0(0) | 0(0) | 0(0) | NA |
| Excision | 2(7) | 4(23) | 4(12) | 2(1) | 0(0) | 1.97(0.82; 4.69) |
| Excision and autograft | 89(335) | 91(515) | 93(299) | 95(60) | 100(2) | |
| Excision and xenograft | 1(5) | 0(1) | 0(0) | 0(0) | 0(0) | NA |
| Excision and allo allograft | 2(7) | 1(7) | 0(1) | 0(0) | 0(0) | NA |
| Type of skin graft | 27(59) | 30(114) | 21(44) | 31(12) | | |
| 1:2 | 51(113) | 58 (218) | 51(108) | 28(11) | | 0.97(0.60; 1.55) |
| **1:4** | 1(3) | 1(2) | 1(3) | 0(0) | | |
| 1:6 | 21(47) | 11(40) | 27(57) | 41(16) | | 0.56(0.12; 2.51) |
| Sheet | 33(20 to 60) | 40(27 to 62) | 55(35 to 87) | 57(31 to 100) | | 0.81(0.49; 1.33) |
| Wound healing time | 10(5 to 19) | 10(6 to 17) | 7(3 to 16) | 10(4 to 16) | 19 (10 to 28) | **1.15(1.02; 1.29)** |
| Excision and grafting timing | 10 (5-19) | 10 (6-17) | 7 (3-16) | 10 (4-16) | | 9 0.90(0.79; 1.02) |

**Table 3**. Sensitivity analysis

| Node | Mutual Information (%) | Variance of beliefs (%) |
|---|---|---|
| Type of surgical approach | 8.75 | 11.7 |
| Number of surgical procedures | 8.09 | 10.9 |
| Burn Treatment | 8.05 | 10.9 |
| Excision and coverage timing | 5.61 | 7.53 |
| Type of skin graft | 3.94 | 5.24 |
| Wound healing time | 3.04 | 4.18 |
| Burn Area | 0.75 | 1.04 |
| Burned Surface Area (BSA) | 0.36 | 0.45 |
| Full Thickness BSA _BSA | 0.1 | 0.13 |
| Age | 0.08 | 0.11 |
| Etiology | 0.023 | 0.032 |
| Sex | 0.02 | 0.031 |

**Table 4.** Predicted probabilities of developing hypertrophic scare along with the probability of observing the hypothesized scenario.

| Patient | Age | Burnt area | Surface area | Full thickness | Probability hypertrophic scare (%) | Probability of evidence (%) |
|---|---|---|---|---|---|---|
| 1 | <15; | Abdomen; | <23 | <19 | 56.6 | 6.49 |
| 2 | 15-65; | Upper limb | <20 | <33 | 60 | 22.11 |
| 3 | >65 | Lower limb | <30 | <19 | 53.8 | 2.39 |
| 4 | <15; | Neck | <23 | >57 | 69.9 | 1.01 |
| 5 | 15-65; | Upper limb | 23-47 | >57 | 66.9 | 2.12 |
| 6 | >65 | Neck | > 72 | >57 | 54.1 | 1.38 |
| 7 | <15; | Upper limb | <23 | <19 | 62.6 | 3.38 |
| 8 | 15-65; | Upper limb | >72 | 38-57 | 98.6 | 0.12 |
| 9 | >65 | Upper limb | > 72 | <19 | 51.8 | 1 |

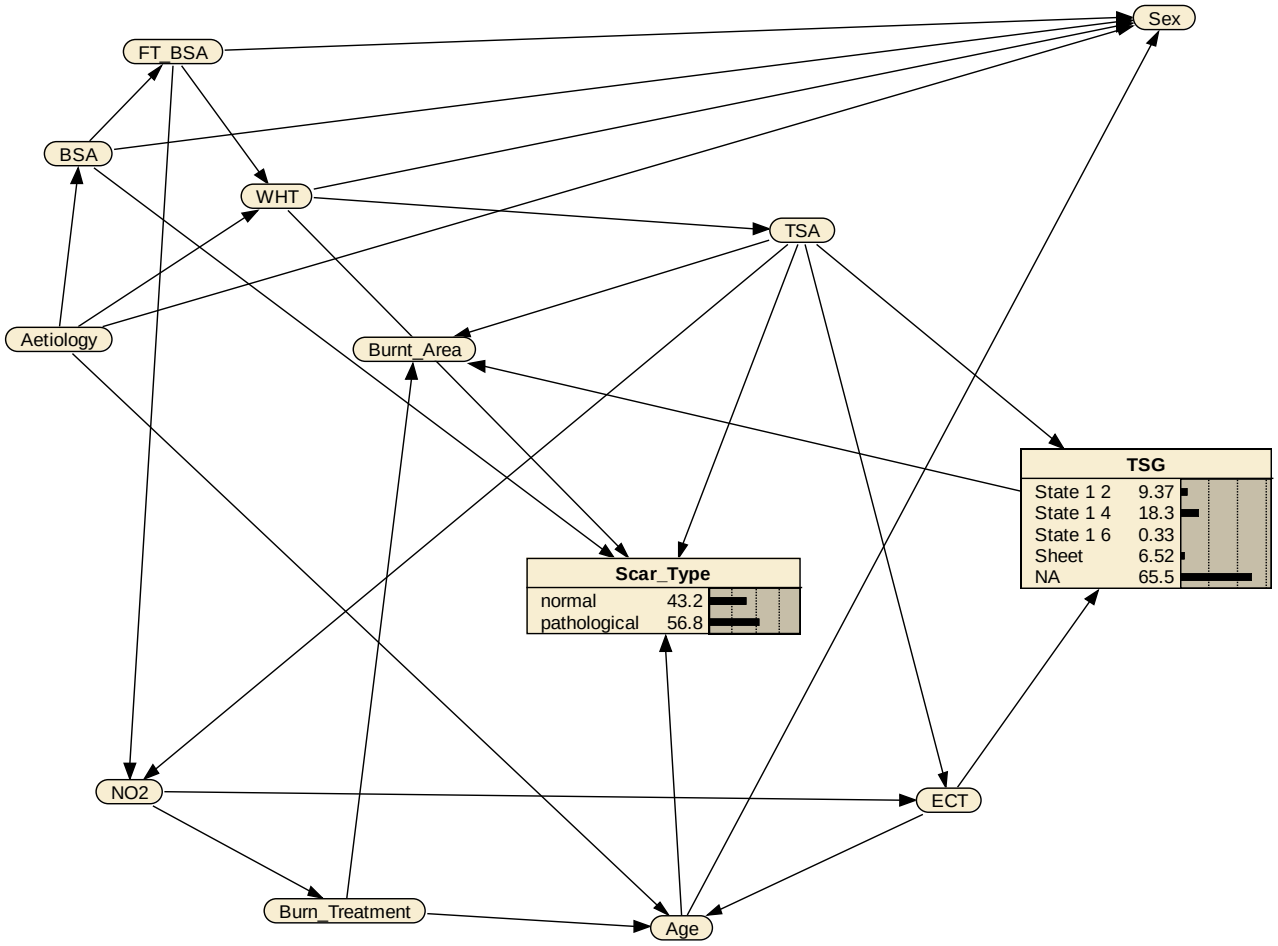


**Figure 1**. BN structure along with probability distributions