Development of a Predictive Calculating Stroke Risk tool using the new Framingham Stroke Risk Profile

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Contents

Abstract

The incidence of stroke adjusted for age has declined over the last half-century, most likely due to alterations in the prevalence and influence of numerous risk factors associated with stroke. The Framingham Stroke Risk Profile may more accurately predict current hazards in the Framingham Heart Study and other cohorts. A health risk appraisal function has been developed to predict strokes using the Framingham Study cohort. The stroke risk factors included in the profile are age, systolic blood pressure, the use of antihypertensive therapy, diabetes mellitus, cigarette smoking, prior cardiovascular disease (coronary heart disease, cardiac failure, or intermittent claudication), atrial fibrillation, and left ventricular hypertrophy by electrocardiogram. On the basis of this information, an Excel program was created, and 45 cases were examined to determine the ten-year stroke risk factor. An individual's risk can be related to the average risk of stroke for persons of the same age and sex. The information that one's risk of stroke is several times higher than average may provide the impetus for risk factor modification. It may also help to identify persons at substantially increased stroke risk resulting from borderline levels of multiple risk factors, such as those with mild or borderline hypertension, and facilitate multifactorial risk factor modification.

Chapter One

Introduction

Stroke is a significant contributor to disability among individuals aged 60 and above and ranks as the third most prevalent cause of mortality in the United States. In the face of an elderly population of increasing size, stroke is likely to be responsible for even greater disability and death (Feigin et al., 2017). Therefore, tools like Framingham Stroke Risk (FSR) for early stroke prediction are required for the prevention of strokes. The FSR Profile is the most extensively utilized tool for predicting the risk of stroke. It is used in physician offices to educate patients and strategize treatments and has been recommended by the American Heart Association. It is utilized in scientific environments to evaluate the additional predictive capacity of imaging, circulating, genetic, or biomarkers (Parmar et al., 2015, Dufouil et al., 2017).

The birth of the Framingham Stroke Risk Profile (FSRP) was initially documented in 1991 (Wolf et al., 1991). The model incorporates the impact of age, sex, and initial measurements of different vascular risk factors, including systolic blood pressure (SBP), use of antihypertensive medications, presence or absence of left ventricular hypertrophy on electrocardiography (ECG-LVH), existing cardiovascular disease (CVD), current smoking status, and current or previous atrial fibrillation (AF) and diabetes mellitus (DM), to describe a 10-year probability of incident stroke. Therefore, in a 70-year-old man with increased levels of 1 risk factor and an SBP of 160 mmHg, the risk might range from 8% when there are no other risk factors present to 85% when all 6 risk factors are present. The assignment of an aggregate FSRP score is determined by the hazard ratio (HR) associated with each individual stroke risk factor and the presence or absence (or levels) of those factors (Ridker and Cook, 2004, Allan et al., 2012, Homayoon et al., 2013).

Despite this, a number of studies, including those that utilized data from the Framingham cohorts, have shown that the age-adjusted incidence of stroke has decreased over the last half-century, including the three decades that have passed since the FSR profile originated (Anderson et al., 2005, Carandang et al., 2006). Evidently, the FSR profile overestimated risk when applied to a French study conducted in the early 2000s; the REGARDS study (Reasons for Geographic and Ethnic Differences in Stroke) has confirmed this (Bineau et al., 2009). Several factors may have contributed to this overestimation, including population differences (genetic and lifestyle differences may have decreased the risk of stroke in France relative to the United States) and the application of an obsolete risk profile to a more recent sample. Since the FSRP was first described 25 years ago, stroke rates and the prevalence of several risk factors for stroke have decreased, while the efficacy of stroke preventive treatments has increased. This suggests that the latter hypothesis is more possible (Carandang et al., 2006, Menon et al., 2015). This study proposes a tool, the FSR, for predicting the risk of stroke over a ten-year period. The tool's validity is then assessed using 45 participants.

Chapter Two

Materials and Methods

2.1 Materials

2.1.1 Equipment and Instruments

The materials used in this study include Microsoft excel and the Omron M2 basic blood pressure monitor. Excel is a Microsoft-developed spreadsheet editor that is compatible with Windows, macOS, Android, iOS, and iPadOS. It includes pivot tables, calculation or computation capabilities, and graphing tools (Bothell, 2023). The Omron M2 basic blood pressure monitor was also utilized, as it aids in the diagnosis and monitoring of hypertension, aids in the detection of cardiovascular risk, and provides a more comprehensive picture of heart health. This monitor measures blood pressure and detects abnormal heartbeats (Omron, 2007).

2.1.2 Data Collection of Stroke Risk Factors

In 45 randomly selected subjects (20 men and 25 women), the 10-year probability of suffering a stroke was calculated. Age and systolic blood pressure, the presence or absence of specific risk factors for stroke, and the concentrations of these risk factors were collected from information gathered at each baseline examination. The study participants (Table 1) had an average age of 37 ± 15.52 for men and 36.84 ± 17.35 for women. Blood pressure is another important measurement taken during this research. Hence, brachial blood pressure, including SBP alone, was three times measured and averaged with a sphygmomanometer, a non-invasive blood pressure method, following a 10-minute rest using automated digital equipment (Omron M2 Basic Automatic Monitor). Hence, their systolic blood pressure was 121.8 ± 10.6 and 123.2 ± 12.1, respectively. Other parameters collected via yes-or-no questions include hypertension medication, diabetes mellitus, current smoking status, cardiovascular disease, and atrial fibrillation.

Table 1. Features of the study participants

Parameters	Men	Women	Unit
Age	37 ± 15.52	36.84 ± 17.35	Years
SBP	121.8 ± 10.6	123.2 ± 12.1	mmHg
Hypertension medication	2 Yes, 18 No	4 Yes, 21 No	Yes or No
Diabetes mellitus	6 Yes, 14 No	8 Yes, 17 No	Yes or No
Current smoker	16 Yes, 4 No	1 Yes, 24 No	Yes or No
CVD	2 Yes, 18 No	3 Yes, 22 No	Yes or No
Atrial Fibrillation	0 Yes, 20 No	1 Yes, 24 No	Yes or No

2.2 Method

The proposed methodologies for calculating the 10-year stroke risk as a computer aided diagnosis will be explained based on the new Framingham risk. Two Excel programs, one for men and one for women, were proposed to predict the risk of stroke over the next decade using the new Framingham risk stroke.

2.2.1 Computational Details

The following information provides computational specifics to calculate the new FRS profile based on individual-specific risk factor values. The probability of stroke at time t is estimated as (Dufouil et al., 2017):

$$\boldsymbol{FSRP(t) = 1 - S_b(t)^{\exp(L-M)}} \dots\dots\dots\dots\dots\dots (\mathbf{1})$$

Where $S_b(t)$, the baseline survival at time t, is the probability of survival free of stroke at time t, for an individual whose risk factor values are equal to the sample mean values of those risk factors. The expression can be understood as the likelihood of surviving while accounting for the influence of the risk factors incorporated in the model. This is in contrast to the Kaplan-Meier survival estimate, which essentially ignores the risk factor. $L = \sum_i (\beta_i \, x_i)$ is the linear combination of individual's risk factor values and the corresponding coefficients estimated using Cox proportional hazards regression. M is simply L calculated using the mean of all covariates; it is presented in Table 2, along with the beta coefficients required to compute L (Dufouil et al., 2017, Wolf et al., 1991).

Table 2. The components needed to calculate the FSRP: β coefficients, means of the risk factors (prevalence for binary variables), M, and $S_b(10)$, baseline survival at 10 years.

	Men		Women	
	β	Mean	β	Mean
Age per 10 years	0.49716	6.6753	0.87938	6.787
Current SMK	0.47257	0.1244	0.51127	0.1384
Prevalent CVD	0.45341	0.1798	- 0.0303	0.10068
Prevalent AF	0.0806	0.0707	1.2072	0.032
Age 65+	0.4542	0.5229	0.3979	0.5681
DM, if age<65	1.3530	0.0584	1.0711	0.0320
DM, if age 65+	0.3438	0.0921	0.06565	0.05645
HTN Rx	0.8259	0.4212	0.1308	0.3969
SBP per 10, if no HRx	0.2732	0.6656	0.1130	0.5706
SBP per 10, if HRx	0.0979	0.8152	0.1723	0.9388
$\boldsymbol{L} = \sum_i(\boldsymbol{\beta_i}\, \boldsymbol{x_i})$, evaluated at the mean of the risk factors		4.4227101		6.6170719
$S_b(10)$		0.94451		0.95911

AF indicates atrial fibrillation (yes/no); BP, blood pressure; CVD, prevalent cardiovascular disease (yes/no); DM, diabetes mellitus (yes/no); HRX, hypertension medications; SBP, systolic blood pressure; and SMK, current smoking (yes/no).

Table 3. Baseline survival, $S_b(t)$, for t=1…10.

t	$\boldsymbol{S_b(t)}$	
	Men	**Women**
1	0.99598	0.99901
2	0.99478	0.99697
3	0.98919	0.99424
4	0.98531	0.99074
5	0.98059	0.98710
6	0.97661	0.98327
7	0.96983	0.97890
8	0.96179	0.97326
9	0.95509	0.96581
10	0.94451	0.95911

2.2.1.1 Computation for Women

For women, $M = 6.6170719$, $S_b(10) = 0.95911$, and the Framingham stroke risk (FSR) of women for ten years can be found using equation 2.

$$\boldsymbol{FSR(10) = 1 - (0.95911)^{\exp(L-6.6170719)}} \dots\dots\dots\dots\dots\dots \mathbf{(2)}$$

But, the linear combination (L) is needed and can be calculated as follows (equation 3):

$$\begin{aligned} \boldsymbol{L} = {} & \mathbf{0.87938} \times (\boldsymbol{Age}/\mathbf{10}) + \mathbf{0.51127}\ (\boldsymbol{if\ SMK}) - \mathbf{0.03035}\ (\boldsymbol{if\ CVD}) + \mathbf{1.20720}\ (\boldsymbol{if\ Af}) \\ & + \mathbf{0.39796}\ (\boldsymbol{if\ Age} \geq \mathbf{65}) + \mathbf{1.07111}\ (\boldsymbol{if\ Age} \\ & < \mathbf{65}\ \boldsymbol{and\ DM}) + \mathbf{0.06565}\ (\boldsymbol{if\ Age} \geq \mathbf{65}\ \boldsymbol{and\ DM}) + \mathbf{0.13085}\ (\boldsymbol{ifHRX}) \\ & + \mathbf{0.11303} \times (\boldsymbol{SBP} - \mathbf{120})/\mathbf{10}\ (\boldsymbol{if\ no\ HRX}) + \mathbf{0.17234} \times (\boldsymbol{SBP} \\ & - \mathbf{120})/\mathbf{10}\ (\boldsymbol{if\ HRX}) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots \mathbf{(3)} \end{aligned}$$

2.2.1.2 Computation for Men

For men, $M = 4.4227101$, $S_b(10) = 0.94451$, and the FSR of men for ten years can be found using equation 4.

$$\boldsymbol{FSR(10) = 1 - (0.94451)^{\exp(L-4.4227101)}} \dots\dots\dots\dots\dots\dots \mathbf{(4)}$$

But, the linear combination (L) is needed and can be calculated as follows (equation 5):

$$\begin{aligned} \boldsymbol{L} = {} & \mathbf{0.49716} \times (\boldsymbol{Age}/\mathbf{10}) + \mathbf{0.47254}\ (\boldsymbol{if\ SMK}) + \mathbf{0.45341}\ (\boldsymbol{if\ CVD}) + \mathbf{0.08064}\ (\boldsymbol{if\ Af}) \\ & + \mathbf{0.45426}\ (\boldsymbol{if\ Age} \geq \mathbf{65}) + \mathbf{1.35304}\ (\boldsymbol{if\ Age} \\ & < \mathbf{65}\ \boldsymbol{and\ DM}) + \mathbf{0.34385}\ (\boldsymbol{if\ Age} \geq \mathbf{65}\ \boldsymbol{and\ DM}) + \mathbf{0.82598}\ (\boldsymbol{ifHRX}) \\ & + \mathbf{0.27323} \times (\boldsymbol{SBP} - \mathbf{120})/\mathbf{10}\ (\boldsymbol{if\ no\ HRX}) + \mathbf{0.09793} \times (\boldsymbol{SBP} \\ & - \mathbf{120})/\mathbf{10}\ (\boldsymbol{if\ HRX}) \dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots\dots \mathbf{(5)} \end{aligned}$$

The tools were built by inputting equations 2, 3, 4, and 5 into Excel with the purpose of calculating the 10-year stroke risk using the Framingham profile. Thus, a total of 45 participants (20 males and 25 females) underwent examination using the tools.

Chapter Three

Results and Discussion

Two Excel programs as a computer aided diagnosis (Fig. 1) were developed based on the new Framingham stroke risk assessment, one specifically designed for men and another for women. These programs aim to accurately forecast the likelihood of experiencing a stroke within the next ten years. Hence, such tools are crucial for early stroke prediction because early detection of the condition can potentially save a patient's life. According to (Kaur et al., 2022), in 85 percent of cases, mortality and severe brain damage can be averted with early detection or diagnosis of stroke and can avoid disability and loss of life.

Framingham Risk Factors for stroke	Units	(Type Over Placeholder Values in Each Cell)
Gender	Female (F)	F
Age	years	57
SBP	mm Hg	135
Hyp_Rx	yes (y) or no (n)	n
DM	yes (y) or no (n)	n
current smoker	yes (y) or no (n)	n
CVD	yes (y) or no (n)	n
AF	yes (y) or no (n)	n
Time Frame for Risk Estimate	10	
L is the Linear combination		5.182011
10 years risk		0.009891349

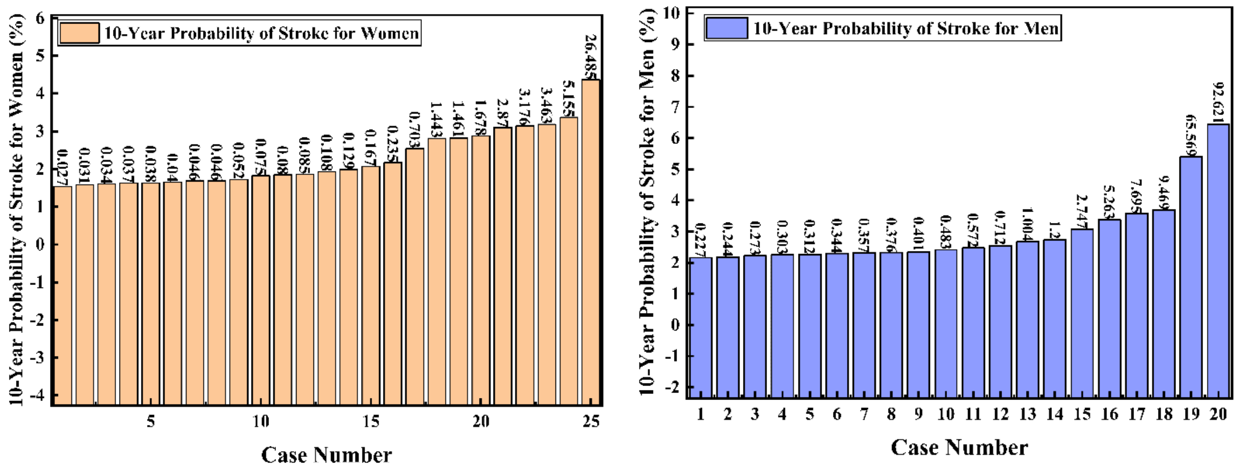
(a)

Framingham Risk Factors for stroke	Units	(Type Over Placeholder Values in Each Cell)
Gender	Male (m)	M
Age	years	57
SBP	mm Hg	135
Hyp_Rx	yes (y) or no (n)	n
DM	yes (y) or no (n)	n
current smoker	yes (y) or no (n)	n
CVD	yes (y) or no (n)	n
AF	yes (y) or no (n)	n
Time Frame for Risk Estimate	10	
L is Linear combination		3.243657
10 years risk		0.017405598

(b)

Fig. 1 Designed Excel tools for **a)** women and **b)** men.

After the completion of the programs, 45 participants, including 20 males and 25 females, were examined to determine their risk of having a stroke in ten years based on factors such as age, systolic blood pressure (SBP), atrial fibrillation (AF) (yes/no), prevalent cardiovascular disease (CVD) (yes/no), diabetes mellitus (DM) (yes/no), hypertension medications, and current smoking (yes/no). The risk of stroke, as estimated by Framingham, is depicted in Figure 2 for the 45 subjects who took part in this research. One aspect to consider is that the minimum 10-year stroke risk for women is 0.027%, as illustrated in Figure 2a. The maximum probability, on the other hand, is 26.48%. As shown in Figure 2b, the minimum 10-year risk of stroke for men is 0.227 percent, which is greater than the minimum 10-year risk for women in this study. In addition, it has been found that in this study, men have a greater maximum 10-year probability of stroke risk, at 92.621%, compared to women. Furthermore, the second highest chance of a stroke in men during 10 years is 65.569%, indicating a significant risk.



(a) **(b)**

Fig. 2 10-year probability of stroke for 45 participants a) 25 women and b) 20 men.

In this study, the main factors that contribute to the risk of stroke include age, SBP, AF, CVD, DM, hypertension medications, and current smoking. Individuals who are at a higher risk of stroke are those who are older and have high SBP, as well as CVD and DM. The study finds that men have a higher 10-year risk of stroke compared to women (Fig. 2). This difference can be attributed to the fact that a majority of male participants in the study reported smoking (Table 1), whereas one woman engaged in smoking.

Program validation is a highly vital aspect. Thus, the Excel tools were validated using two examples mentioned in (Dufouil et al., 2017) that pertain to both men and women. The probability of the stroke risks for these genders were calculated to be 0.0098 and 0.0174, respectively. By running our programs on the same examples with the same parameters given in (Dufouil et al., 2017), the proposed programs gave the same outcome as shown in Figures 1a and b.

Chapter Four

Conclusion and Future Work

This study proposed two Excel programs as a computer aided diagnosis for men and women with the purpose of forecasting the risk of stroke in ten years, utilizing the newly updated Framingham stroke risk. The designed programs involved the utilization of mathematical equations to compute the probability of stroke risk based on seven parameters: age, SBP, AF, CVD, DM, hypertension medication, and smoking. Following that, 45 subjects, 25 women and 20 men were subjected to the programs in order to determine the ten-year risk of stroke. This study provides evidence that the risk of stroke is increased by all of the factors considered. Men are more likely than women to be at elevated risk for stroke in this study; this is because the majority of men who participated in the research are smokers or have CVD. In order to validate the programs, they were evaluated using two provided examples and the results were compared. In the future, a larger cohort of stroke patients can be subjected to testing using these algorithms. The tools can be enhanced by integrating them with other software, such as MATLAB or Python, to increase their sophistication and transform them into graphical user interfaces (GUI). This would enable the tools to be used as applications on smartphones, which would be particularly valuable for individuals at risk of stroke.

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