Biological and psychological factors associated with smoking abstinence six years post-stroke

Title page

Authors

Rosa Suñer-Soler. PhD. Nursing Department. University of Girona (Spain) (corresponding author) rosa.sunyer@udg.edu
Author information: Fax number: 0034 972418773 Telephone number: 0034 972418770

Armand Grau-Martín. PhD. Fundació Salut Empordà and Quality of Life Research Institute, University of Girona (Spain)
grauma@comg.cat

Mikel Terceno. MD. Neurology, Hospital Universitari Dr. Josep Trueta (Spain)
Mikelterceno@hotmail.com

Yolanda Silva. PhD. Neurology. Hospital Universitari Dr. Josep Trueta de Girona (Spain)
Ysilva.girona.ics@gencat.cat

Antoni Davalos. PhD. Prof. Neurosciences Department . Universidad Autónoma de Barcelona (Spain)
adavalos.germanstrias@gencat.cat

Juan Manuel Sánchez. PhD. Chemistry Department. University of Girona (Spain)
juanma.sanchez@udg.edu

Silvia Font-Mayolas. PhD. Quality of Life Research Institute. University of Girona (Spain)
Silvia.font@udg.edu

Eugenia Gras. PhD. Quality of Life Research Institute. University of Girona (Spain)
Eugenia.gras@udg.edu

Joana Rodrigo. RN. Neurology. Hospital Universitari Dr. Josep Trueta (Spain)
Jrodrigo.girona.ics@gencat.cat

Martha Kazimierczak. RN. Hospital Universitario Marqués de Valdecilla (Spain)
martha.kazi@gmail.com

Carmen Malagón. PhD. Nursing Department.University of Girona (Spain)
Carme.malagon@udg.edu

Joaquín Serena. PhD. Neurology. Hospital Universitari Dr. Josep Trueta (Spain)
Jserena.girona.ics@gencat.cat

Abstract

Introduction. Tobacco use is a public health problem causing high morbidity and mortality, including stroke. This study evaluates predictive factors of smoking cessation in the long term after stroke. **Methods.** We followed a cohort of 110 consecutive smokers with stroke for up to six years. Sociodemographic variables, stroke severity, insular involvement, stage of change in smoking habit before stroke and disruption of addiction variable (smoking cessation , absence of relapses, having stopped smoking without difficulties and not having had urge) were evaluated. **Results.** Twenty patients died during follow-up and two patients were lost leaving a final cohort of 88 patients. The prevalence of smoking cessation in the remaining population was 65.9% post-stroke, 54.9% at three-six months, 40.9% at one year and 37.5% at six years. Prevalence was significantly higher in patients with insular involvement during the first year of follow-up, but not at six years. Disruption immediately after stroke (OR=10.1; 95% CI: 2.5-40.1) and intention to change before having the stroke (OR=4.8; 95% CI: 1.0-23.0) were predictors of abstinence at six years after adjusting for age, sex and stroke severity at baseline. When tobacco abstinence at the one year follow-up was included in the model, this factor was the best predictor of tobacco abstinence at one year (OR=10.5; 95% CI: 2.2-49.4). **Conclusions.** Intention of change, having the disruption criteria, and abstinence one year after stroke were predictors of abstinence at 6 years. An insular lesion in the acute phase of stroke does not determine the tobacco use status at six years.

Implications

This study is the first prospective investigation with a cohort of stroke patients to examine the long-term influence of biological and psychological factors on smoking cessation. Tobacco abstinence one year after stroke was the strongest predictor of abstinence at six years of follow-up. The effect of the insular cortex lesion on tobacco cessation, which had been relevant during the first year, no longer had an influence over the longer period studied here.

Main Text

INTRODUCTION

Tobacco continues to be a main public health problem and represents a serious risk for health worldwide with an estimated six million deaths every year being attributed to causes associated with its use.[1] In 2000, tobacco was responsible for 11% of cardiovascular disease deaths in the world, 25% of these were due to cerebrovascular disease.[2] Tobacco provokes vascular morphological and functional alterations and negatively affects the lipid profile. Furthermore, it decreases the capacity of oxygen transport in the blood. One serious consequence of its action mechanism is that it activates atherogenesis in the coronary and cerebral arteries, which is an important risk factor for acute myocardial infarction and stroke.[3,4,5] Smoking cessation leads to prolonged improvements in endothelial function, which may mediate in the risk of cardiovascular disease.[4] For this reason, helping people to stop smoking is a good primary and secondary prevention measure for stroke. However, the extent to which this is pursued through programs and cessation advice is still limited due to economic and healthcare organizational reasons, lack of knowledge on the part of professionals, and resistance on the part of patients.[1,6,7]

In order to be able to treat smokers who have suffered a stroke and to achieve greater success in secondary prevention, it is important to know the main variables associated with the cessation of smoking post-stroke, such as older age,[8-10] female sex,[11,12] having at least ten years of education,[13] not living alone,[12,13] not being exposed to tobacco at home,[13] having greater functional dependence,[12,14,15] not suffering from depression,[8] less desire to smoke,[10,16]

considering stopping smoking before stroke or a stage of change of contemplation or preparation[17] and insular cortex damage as a result of the stroke.[16-18] Studies of the probable role of the insula in the conscious impulse to consume drugs[16,19-23] have found that an insular cortex lesion due to stroke can cause a loss of desire to smoke, resulting in greater abstinence from smoking,[16-18] although other authors have not found this association.[24]

The objectives of the present study are to find out the evolution in the consumption of tobacco in a cohort of smokers that presented an episode of stroke and who were followed for six years, to compare the quality of life of patients who had given up smoking and those who continued to smoke, and to study the predictive factors in smoking cessation six years after having a stroke.

METHODS

Between January 2005 and July 2007, we studied 110 consecutive patients with an acute stroke of any type who were smokers at the moment of the stroke event. All patients or relatives signed informed consent. The study protocol, was approved by the hospital's Ethics Committee. Six years after stroke, sociodemographic variables (age, sex, living with their family, living with smokers), stroke severity evaluated by the NIH Stroke Scale (also recorded on hospital discharge),[25] functional outcome measured by the Barthel index[26] and the modified Rankin scale[27], stroke recurrence, and the incidence of other diseases related to tobacco use were recorded. Regarding the history of tobacco use, the stage of change in the smoking habit was estimated according to the Transtheoretical Model (retrospectively before stroke, on discharge, at three-six months, one year and six years). Smoking cessation was defined as

being in the Action stage (24 hours to six months without smoking), in Maintenance (from six months to three years) and Termination (from three years without smoking).[28] Furthermore, the disruption of addiction variable, defined by Naqvi et al.[16] as the presence of smoking cessation from the moment of the stroke, the absence of relapses, having stopped smoking without difficulties (<3 on the scale of difficulty) and not having had the urge to smoke since the moment of having stopped smoking, was studied at three-six months. In patients who continued smoking, the daily consumption of cigarettes and the level of tobacco dependence, was recorded, using the shortened Fagerström Test for Nicotine Dependence,[29] (scoring from 0, lowest level of dependence on nicotine, to 10, highest level of dependence). In non-smokers, the number of days of abstinence were registered.

Perceived health-related quality of life was studied through the EQ-5D questionnaire (EQ-5D), validated for a Spanish population.[30,31] The EQ-5D evaluates five domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The responses for the five dimensions can be combined as a five-digit number describing the respondents' health status, and may be converted into a single index value. Furthermore, the EQ-5D also has a vertical, 0-100 point visual analogue scale (EQ VAS) for rating general health status.

Procedure

Patients were studied during hospitalization, at three-six months and one year after stroke at outpatients' visits and at six years either at outpatients' or by telephone. The protocol followed is fully described in a previous publication of our group. [17] An attempt was made to contact all the 110 patients who were initially included in the study to invite them to a neurological visit six years after

their stroke event. 20 of the original 110 were found to have died and two were lost to follow-up (it was not possible to make contact). Those who stated that they could not attend were interviewed by telephone by members of the research team with certification to evaluate the Rankin scale over the telephone. Their neurological status was determined by the data of the patients from their clinical records by general practitioners or neurologists. Those who did attend the visit were evaluated by a neurologist and a research nurse .The levels of specific respiratory biomarkers of tobacco consumption were measured[32,33] through the analysis of benzene and 2,5-dimethyllfuran levels in the breath using chromatographic analysis. Furthermore, the electronic medical histories of all patients or, when necessary, the general practitioner, were consulted to contrast clinical data.

Statistical analysis

The Student T test and the Mann-Whitney U test were used to compare groups in the case of continuous variables and the Chi-square test was used for categorical variables. Two logistic regression analyses were performed to assess variables predicting smoking cessation six years after stroke diagnosis. In the first model, demographic variables (age and sex) and stroke severity (NIHSS) at discharge, the stage of change in smoking habit before stroke, insular involvement of stroke and the existence of the disruption criteria between three and six months after stroke were included. In the second model, an evolving variable called “smoking cessation at one year” was added. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated.

RESULTS

Of the 88 participants who were evaluated at six years after stroke, 54 (61.4%) were interviewed by telephone and 34 (38.6%) were evaluated at a face-to-face visit with a neurologist. Those patients who had died were older than those evaluated at six years (see Table S1 in the Supplementary appendix).

The characteristics of the 88 subjects studied at six years from stroke are set out in Table 1. Specifically, the subgroup of patients with insular lesions compared with patients without insular lesions had similar sociodemographic characteristics (sex, age, living with their family, and living with smokers), however, they had greater neurological damage (median NIHSS of 2; $p< 0.001$), worse functional state (median Rankin of 2.5; $p=0.008$) and less autonomy (median Barthel of 90; $p=0.002$).

Among the 88 patients who completed the six-year follow-up, the prevalence of smoking cessation was 48/88 (54.5%) at three-six months, 36/88 (40.9%) at one year and 33/88 (37.5%) at six years. Breath analysis tests found complete coincidence in patients who attended the visit between the presence of 2,5-dimethylfuran, an indicator of having smoked in the past 24 hours, and self-declared status as active smokers (n:24). Figure 1 shows the evolving changes in tobacco use at the different time points. Six-years after stroke, 25 (69.4%) of the 36 patients that were not smoking at one year continued to be abstinent, whereas 11 (30.6%) patients relapsed. Among the 52 smokers at one year, 8 (15.4%) had stopped smoking at six years.

With regards to the stage of change six years after stroke, among the active smokers (n: 55; 62.5%) 50 were in the precontemplation stage and five in the contemplation or preparation stage. The average number of cigarettes smoked

per day was 14.6 (SD 12.6) and the average Fagerström test score was 4.5 (SD 2.3). Among the 33 (37.5%) non-smokers, two were in the Action stage, six in the Maintenance stage and 25 in the Termination stage, with an average of 66.6 (SD 31.3) months of abstinence. Characteristics and associated factors in patients who were smokers and non-smokers at six years are shown in Table 1.

In the cohort as a whole, male sex, living in a family setting and living with non-smokers were significantly associated with smoking abstinence at six years. Non-smokers at six years were less frequently in the Precontemplation stage (prior to stroke and one year after the diagnosis). The patients of this sample with insular cortex lesions (n=20) had a higher prevalence of tobacco cessation than patients who were not affected in this area: 95% post-stroke ($p<0.01$), 85% at three-six months ($p<0.01$), 75 % at one year ($p<0.001$) and 45 % at six years ($p>0.05$) (Figure 2). In patients with insular lesions, 100% (n=5) of the smokers at one year continued smoking at six years and 40% (6 out of 15) of the non smokers at one year were active smokers in the control at six years. In this subgroup, the influence of male sex on smoking cessation was not confirmed.

All patients who fulfilled the disruption criteria post-stroke (n=20) continued to be abstinent from tobacco at 12 months after stroke ($p<0.001$) and 80% (n:16) at six years ($p<0.001$) (Figure 2). The probability of fulfilling the disruption criteria was greater in participants with an insular cortex lesion (40%; 8 out of 20) than in participants without damage to this area (17.6%; 12 out of 68) with a relative risk of 2.26 (CI 95%: 1.07 - 4.76).

With regards to perceived health, differences were not observed between smokers and abstainers at six years of stroke in the five dimensions of the EQ-

5D questionnaire. However, non-smokers had better perceived health than active smokers in the visual analogical scale of the EQ-5D (p=0.021) (Table 2). Disruption criteria between three and six months after the stroke (OR=10.1; 95% CI: 2.5-40.1), and the intention to change smoking habits before the stroke (being in the Contemplation or Preparation stage) (OR=4.8; 95% CI: 1.0-23.0), but not the presence of an insular cortex ischemic lesion in the acute phase of stroke (OR=0.9; 95% CI: 0.1-6.4) were independently associated with a greater probability of remaining abstinent at six years after adjustment for age, sex, and an evolving neurological condition (NIHSS at discharge). The first model uses independent variables that can be obtained in the initial history of the patient and in the first months of evolution (Table 3). When abstinence from tobacco consumption at the one year follow-up was included in the model, it was the strongest predictor of tobacco abstinence at six years (OR=10.5; 95% CI: 2.2-49.4) whereas the intention of change before stroke and the disruption criteria after stroke were no longer significant (Table 3).

DISCUSSION

This longitudinal study shows that six years after acute stroke, 37.5% of the patients were abstaining from smoking. This result is similar to that observed by Gall et al.[15] (37%) in following up 51 smokers with acute stroke over a five-year period, and greater to that reported by Ives et al.[14] at three years (30%). Other studies have reported prevalence of smoking cessation in periods of one year or less ranging between 21.7 and 43%.[10-12,24] In our cohort, the prevalence of smoking cessation at one year was 40.9%, which means that among survivors six-years after stroke (20 patients died), only the prevalence of smoking

cessation decreased 3.4%. It should be taken into account, however, that the changes of smoking state took place in both directions. The stages of change following the Transtheoretical Model of Prochaska showed a tendency towards stabilization of the behavior given that most abstainers were in the termination stage whilst almost none of the patients that had continued smoking were considering giving up smoking. Therefore, one year of observation seems to be sufficient to evaluate the full impact of the acute stroke on tobacco use.

A weak association has been found between smoking cessation at six years and male sex, although our study does not allow conclusions to be drawn. The literature does not clarify this subject as contradictory results have been reported.[11,12] Living in a family setting[12] and not living with smokers has also been associated with cessation.[13]

The overall perception of health was better among patients who stopped smoking than among active smokers, although there were no differences in the quality of life domains of the EQ-5D between the two groups. Other longitudinal studies in the general population[34] and in people with physical disabilities[35] have shown an evolving improvement in the perception of health in smokers that stopped smoking in comparison with those that continued smoking. In patients with atherosclerosis related diseases, a significantly better perception of health,[36] a mild improvement that did not reach significance[37] or no differences[38,39] have been found in participants who stopped smoking in comparison to those who did not. Cross-sectional studies of the general population have shown better perception of health among ex-smokers in comparison with active smokers.[40-44]

With regards to the effect of smoking cessation on mental health, a meta-analysis of 26 studies showed that anxiety, depression and stress diminished significantly after smoking cessation, improving mood and quality of life.[45]

In the present cohort, the stage of change before stroke reported at baseline was a good predictor of tobacco cessation at six years. We have also observed that although the insular cortex lesion was found to lose its predictive capacity in the long term, the presence of disruption criteria in the first six months post-stroke allowed better cessation results to be predicted at the six-year follow-up and the probability of meeting disruption criteria was significantly higher in patients with the insular cortex lesion than in participants without insular cortex damage. Both our previous results[17] and the results published here coincide with those presented by other authors in observing 1) that insular cortex lesions influence tobacco cessation in the short term,[18,46] 2) that there is no long term direct association between insular cortex lesion and tobacco cessation,[16] and 3) that insular cortex damage influences the disruption criteria associated with giving up smoking in the long term.[16]

Tobacco abstinence one year after stroke was the strongest predictor of abstinence at six years of follow-up. This variable was associated with the presence of insular cortex injury and with the intention of giving up smoking before stroke.[17] The first year post-cessation has the greatest risk of relapse but the risk of relapse falls progressively as the length of the period of abstinence increases, resulting in 36% of relapses at two years, 25% after five years and 10% at 30 years of cessation, although the risk never disappears completely.[47]

Our findings allow us to hypothesize that in the acute phase of tobacco cessation after stroke, the neurobiological component and the psychological component of abstinence have an influence on the ability to stop smoking. In this respect the insular lesion may facilitate a successful passage through this early phase in which one's own beliefs and dispositional balance, determining the stage of change, also play a role. This may result in a reduced urgency to smoke immediately after the lesion occurs. In this respect, Abdolahi et al.[18] found in a sample of 156 smokers that patients with insular damage experienced fewer and less severe tobacco withdrawal symptoms, and were less likely to require nicotine replacement therapy during hospitalization than smokers with non-insular damage. In the later stages of the change process, after having overcome the action phase, psychological variables such as the absence of emotional psychopathology,[48] may have a greater influence than neurobiological variables on maintaining abstinence. This could explain the greater prevalence of abstinence in the first year after stroke among patients with insular lesions and/or disruption criteria, and the decrease in the prevalence of abstinence among these patients from one year after stroke,[47] contrasting with the relative stability in tobacco abstinence in the rest of the cohort (Figure 2), who may have been more influenced by psychological factors.

With regards to the limitations of the present study, it should be mentioned that many of the participants only agreed to be interviewed by telephone and that it was not possible to conduct objective proof regarding smoking habits for the whole sample, which would give strength to the validity of the results[49] although

self-reported tobacco cessation has been found to be a reliable and valid method in different studies.[50] Furthermore, the number of participants in the cohort has limited the strength of the multivariate analysis, making it necessary to continue studying tobacco cessation in stroke patients with larger cohorts, and especially in those with insular cortex damage, and also to evaluate the effect of the lesion on other areas indicated in the literature.[46,51-52] A further limitation is that the little repercussion of stroke on the neurological deficit and the functional capacity of the participants could have resulted in it having had less impact on the patients and less influence on them in reflecting on their smoking habit in comparison with people who have suffered larger strokes with more important sequels and dependence. Finally, the exclusion of those patients who had more serious insular lesions may have had an influence on the fact that we did not find insular damage to have an effect on smoking cessation at six years.

In conclusion, despite having suffered a stroke, most patients fail to eliminate tobacco addiction as a risk factor for subsequent stroke, suggesting the need to continue improving the awareness amongst patients of how harmful this habit is. Ex-smokers had a better perception of health than smokers six years post-stroke. We are able to predict a greater probability of abstinence at six years in patients with the intention to change before the stroke or with the disruption criteria after stroke. Furthermore, those who were abstinent one year after stroke had a greater probability of being abstinent at six years.

Taking our results as a whole, we would recommend that the state of change before stroke should always be evaluated in order to identify the subgroup that does not have the intention to change and who will need greater follow-up and

support in order to increase the rates of abstinence from smoking after hospital discharge. An important specific finding is that the effect of the insular cortex lesion on tobacco cessation, which had been relevant during the first year, no longer had an influence over the longer period studied here. As far as clinical practice is concerned, our results suggest that patients with insular lesions, who are mostly abstinent one year after stroke, should be monitored and treated after this period, for example with multimodal therapeutic strategies, in order to avoid relapses, given that 40% started smoking again.

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DECLARATION OF INTERESTS

None declared.

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Table 1. Characteristics of Study Subjects

Variables assessed at follow-up (6 years post-stroke)	All stroke n:88	Smokers n:55 (62.5%)	Non-smokers n:33 (37.5%)	*p*
Age†	60.9±10.9	60±10.4	62.6±11.7	0.28
Sex (Male)	74 (84.1)	43 (78.2)	31 (93.9)	0.05
Living with their family	71 (81.6)	40 (74.1)	31 (93.9)	0.02
Living with smokers	17 (20.7)	14 (28)	3 (9.4)	0.04
Prochaska stage prior to stroke (Precontemplation)	74 (84.1)	51 (92.7)	23 (69.7)	0.00
Prochaska stage 1 year post-stroke (Precontemplation)	28 (31.8)	23 (41.8)	5 (15.2)	<0.00
Disruption At 3-6 months post-stroke	20 (22.7)	4 (7.3)	16 (48.5)	<0.00
Insular damage	20 (22.7)	11 (20)	9 (27.3)	0.43
NIHSS	0 (0-1)	0 (0-1)	0 (0-0.75)	0.32
Barthel Index at follow-up	100 (100-100)	100 (100-100)	100 (92.5-100)	0.57
Rankin Scale at follow-up	0 (0-2)	1 (0-3)	0 (0-2)	0.47

Values are median (25-75 percentiles) or number (percentages)

† Values are means ± SD

Table 2. Tobacco Cessation and Health-related Quality of Life (EQ-5D) in Stroke Survivors

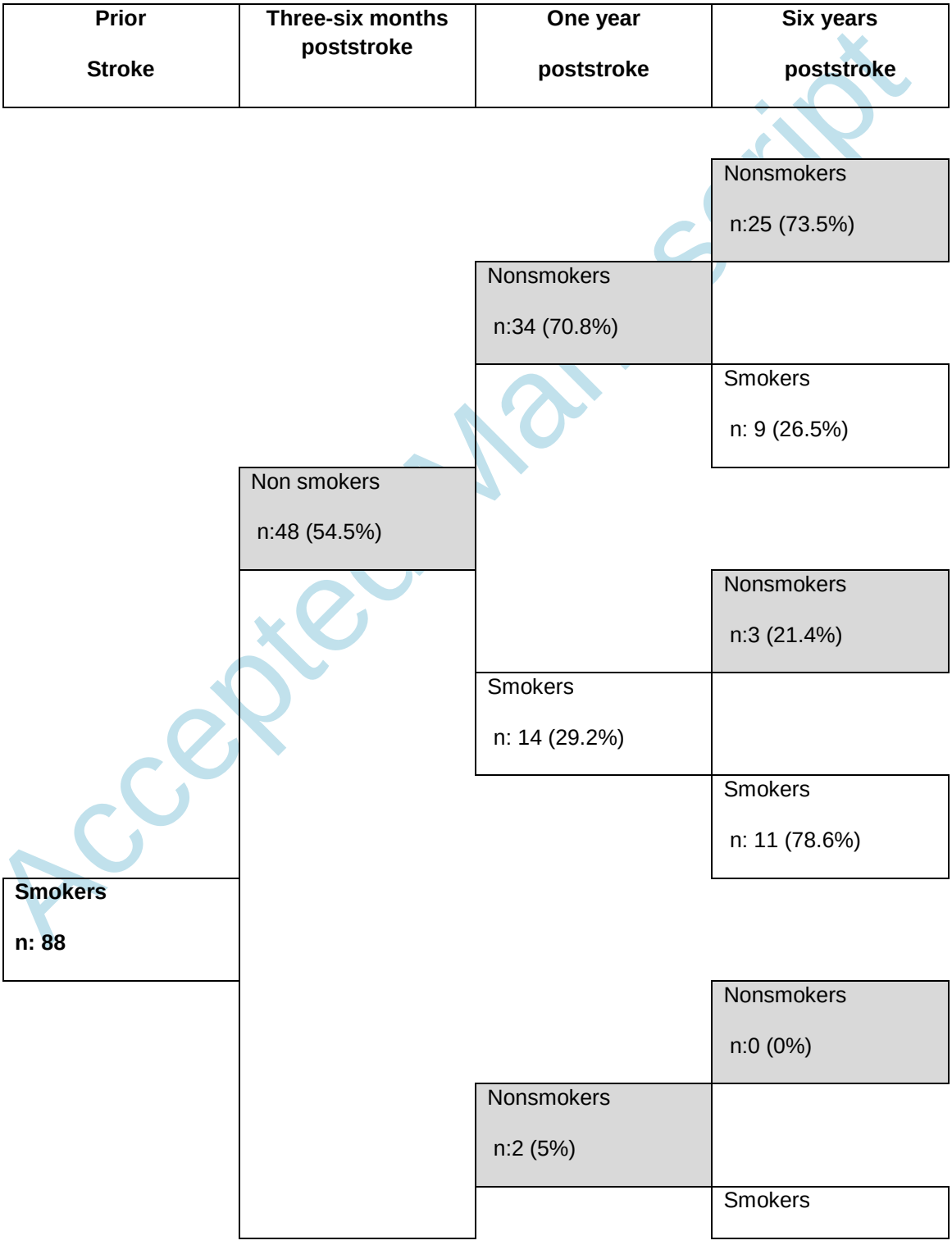
	All stroke n:88	Smokers n:55	Non-smokers n:33	*p*
Mobility problems	31 (35.6)	20 (37)	11 (33.3)	0.72
Self-care problems	24 (27.6)	13 (24.1)	11 (33.3)	0.35
Every day activities problems	34 (39.1)	22 (40.7)	12 (36.4)	0.68
With pain/discomfort	40 (46)	21 (38.9)	19 (57.6)	0.09
With anxiety/depression	35 (40.2)	24 (44.4)	11 (33.3)	0.30
IQ Index†	0.901 (0.702-1.00)	0.910 (0.720 – 1.00)	0.857 (0.695 – 0.966)	0.59
Health-related quality of life (EQ-5D VAS) †	70 (50-80)	62.5 (50-80)	80 (60-85)	0.02

Values are numbers (percentages)
† Values are median (25-75 percentiles)

Table 3. Variables predicting smoking cessation 6 years after stroke diagnosis in multivariate logistical regression analysis

	OR	95% CI	*p*	OR	95% CI	*p*
	First Model			*Second Model*		
Sex (Female)	0.259	0.038-1.769	0.168	0.152	0.018-1.284	0.08
Age	1.019	0.965-1.076	0.493	0.994	0.936-1.057	0.85
NIHSS at discharge	0.998	0.845-1.177	0.978	0.977	0.827-1.153	0.78
Insular damage	0.976	0.149-6.408	0.980	0.499	0.07-3.48	0.48
Intention to change before stroke†	4.817	1.006-23.062	0.049	2.968	0.605-14.551	0.18
Disruption 3-6 months post-stroke	10.185	2.583-40.163	0.001	2.683	0.512-14.052	0.24
Abstinence 1 year post-stroke				10.510	2.235-49.425	0.00

OR indicates odds ratio; CI, confidence interval.
†Intention to change: Patients in Contemplation (intending to stop in the next six months) + Patients in Preparation (considering stopping in the next month with an attempt to do so in the past year)



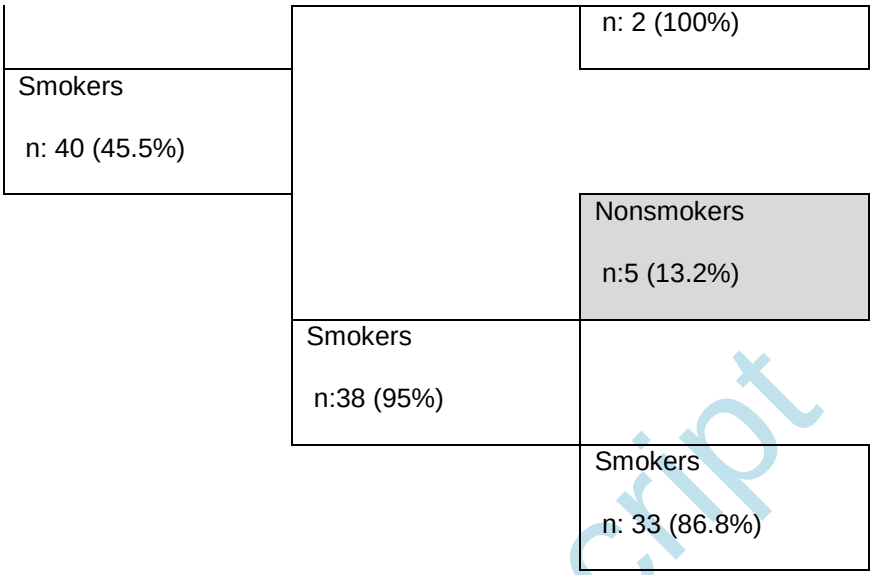


Figure 1 Evolution of smoking status during follow-up

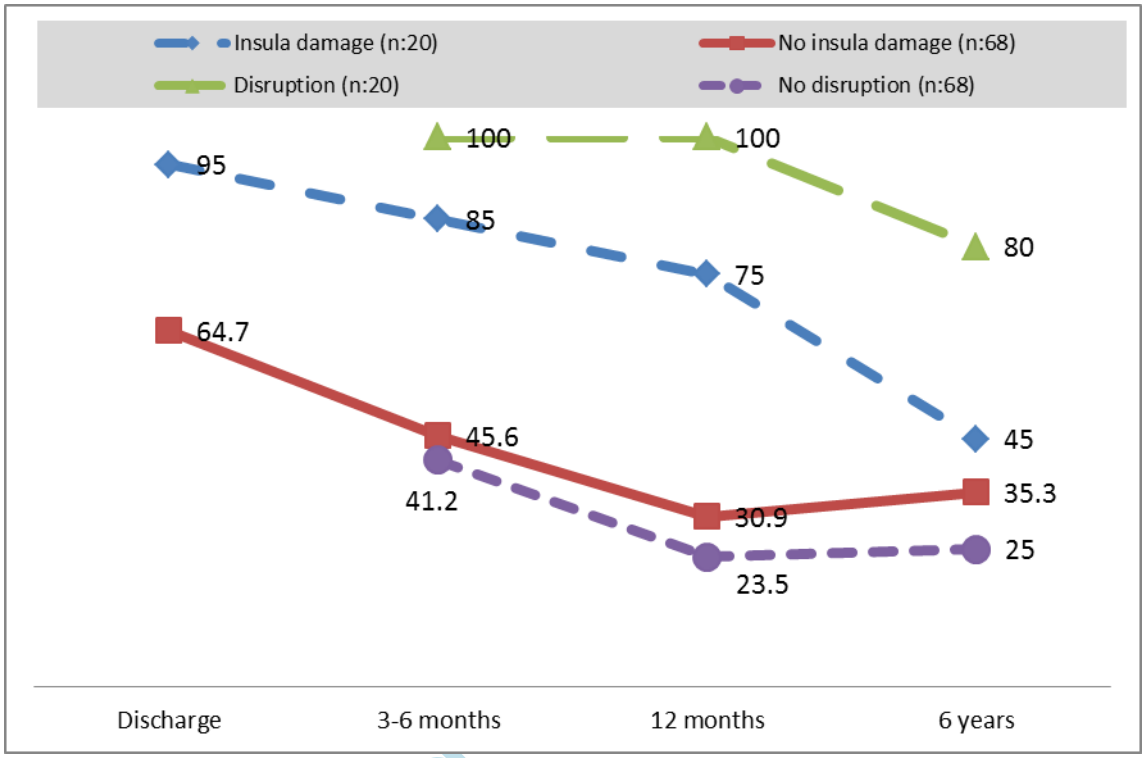


Figure 2 Prevalence of smoking abstinence (%) by presence of insula lesion and meeting of disruption criteria