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Risk factors for prediction of delirium at hospital admittance

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Abstract

Aging population in many developed countries, moves the issue of healthy aging at the forefront of the political, scientific and technological concerns. Delirium is a multifactorial disorder that is highly prevalent in hospitalized elderly people that causes complications in the patient care and increases mortality at the hospital and soon after discharge. Early diagnostics would allow improved treatment and prevention for a syndrome that requires very personalized treatment. This paper deals with machine learning based prediction of delirium at hospital admittance as a computer aided diagnostic tool, as well as with the identification of risk factors by means of the variable importance computed by the classifier model building approaches. We achieve almost 0.80 classification accuracy, which is encourages further exploration of improved classifier models. Exploration of variable importance shows that frailty, dementia and some pharmacological factors are relevant risk factors for delirium at hospital admittance.

KEYWORDS
boosting classification, computer aided diagnosis, delirium, random forest, risk factors

1 | INTRODUCTION

Delirium, aka acute confusional syndrome (ACS), is a neurocognitive disorder of complex aetiology often under-diagnosed that affects the cognitive functionality of the subject (Setters & Solberg, 2017). It is the second more prevalent psychiatric syndrome in the hospital environment (Ohl et al., 2019). Precursors of delirium are anxiety, changes in the sleep cycles and acute changes in attention and consciousness. It is a geriatric syndrome that carries high mortality, longer hospital stays, and loss of cognitive and functional capabilities (Feldman et al., 1999). There are three kinds of clinical instances of delirium: hyperactive, hypoactive and mixed. The most frequent one in older people is the hypoactive (Lipowski, 1987) that shows psychomotor slow down, bradypsychia, slow language, apathy and inhibition. Delirium often imply a preexistent factor and an acute organic disease trigger (Inouye et al., 2014). Causes for delirium encompass a broad spectrum including infection, metabolic disorders, sleep deprival, psychoactive drug abuse, and organic failure (Diwell et al., 2018). Prevalence of delirium in community living elderly is 1%–2%, increasing to 8%–17% in hospital emergency units (Inouye et al., 2014), reaching 10%–31% in hospital stays (Magny et al., 2018). Early diagnostic and treatment is desirable in order to avoid severe worsening of the condition (Avelino-Silva et al., 2017) leading to higher mortality in the following 6 months after discharge (Gower et al., 2012).

Delirium and frailty have been related in some studies (Joosten et al., 2014; Verloo et al., 2016). Frailty is an increasingly prevalent condition as the population is aging in developed countries (Besga et al., 2015; Rodriguez-Mañas & Fried, 2015) and underdeveloped countries (Aboderin & Beard, 2015), recognized as a medical syndrome underlying aging vulnerabilities and ensuing chronic disorders (Vaughan et al., 2015). Frailty identifies a high-risk

subgroup and offers characteristics of great clinical importance: if treated at early stages is more reversible than disability (Ferrucci et al., 1996), and it has high predictive value for adverse outcomes at older ages (Sourial et al., 2013), including delirium after hospital discharge (Verloo et al., 2016).

This paper deals with the prediction of delirium as the main cause for hospital admittance, and the identification of the major risk factors for delirium, some of them associated with frailty of the patients. Machine leaning based predictive model building provides an alternative way to identify the risk factors as the most important variables for predictive performance. Predictive approaches to delirium at hospital admittance cannot resort to deep learning approaches because data is scarce and its rather qualitative nature does not allow for the application of computational data enrichment processes. Hence the state of the art in the literature uses conventional machine learning approaches.

Section 2 describes the recruited cohort and dataset extracted for the computational experiments. Section 3 describes the computational methods. Section 4 reports the computational results. Section 5 provides a discussion of the results. Finally, Section 6 gives some conclusions and lines of future work.

2 | DATASET

The dataset includes patients admitted to the services of internal medicine and neurology at the University Hospital of Alava (UHA), Vitoria, Spain, complying with the following inclusion criteria: age above 70 years, scoring more than 20 in the Mini Mental State Questionnaire (MMSE), ability to walk with or without aids, able to understand and follow simple instruction, and to sign the informed consent. The study has been approved by the ethics committee of the UHA. Patients were excluded for examination if they had any of the following exclusion criteria: history of chronic kidney disease, had suffered a heart attack in the last 3 months, been unable to walk, have suffered any fracture of the upper or lower limbs in the last 3 months, been suffering from severe dementia, a history of autoimmune neuromuscular disorders (e.g., myasthenia gravis, Guillain–Barré syndrome, inflammatory myopathies) or amyotrophic lateral sclerosis, or refused to sign the informed consent. An almost gender balanced cohort of 741 patients where recruited upon admission at the hospital, 170 cause of admittance was delirium. Figure 1 illustrates the recruitment process. Table 1 summarizes the demographic information of the cohort.

Members of the research team with health care experience extracted the electronic health records to extract sociodemographic data, personal antecedent, clinical data, such as comorbidities, and pharmacological treatments. Delirium was diagnosed applying the confusion assessment method (CAM). To assess the functional status of the patient the following tests were applied: Short Physical Performance Battery (SPPB) and Fried's frailty scales and Barthel's scale measuring performance in activities of daily living. The SPPB (Guralnik et al., 1994) includes three tests: balance test, walking speed over four metres, and sitting and stand up five times. Fried's frailty scale (Fried et al., 2001) defines frailty phenotype characterized by involuntary weight loss, fatigue, muscular weakness, slow march, and decay of physical activity. Barthel's scale (Mahoney & Barthel, 1965) measures the physical handicap. The nutritional state was assessed using the mini malnutritional assessment-short form (MNA-SF) as a mean to identify elder subjects at risk of malnutrition before the apparition of severe changes in weight or serum or protein concentrations (Kaiser et al., 2009; Vellas et al., 1999). In order to assess the mental state, the Pfeiffer brief screening test for Dementia (Erkinjuntti et al., 1987; Pfeiffer, 1975) was used. The study collects over 300 variables. Actually, most of the variables suffer from missing values. After careful curation, by setting the default values assumed by the clinician and double checking with the electronic health records, we remove variables with missing values exceeding 20% of the cases. There are some variables that represent the aggregated values of several other variables, that is, the aggregate grades of some tests. We enter both the kind of variables to the variable selection process, thus we might find that some specific component of the test and the aggregated value of the test are significant.

3 | METHODS

In this section we will first give a short description of the classification methods that we have tested for readmission prediction on this frailty dataset. We also detail the classification performance metrics and the complete classifier validation pipeline.

3.1 | Machine learning methods

We have carried out computational validation experiments using several machine learning (Haykin, 1998; Kuhn & Johnson, 2013; Witten et al., 2011) approaches for predictive model building. We have used the Jasp package[1] that is implemented in R but runs independently. We have discarded application of deep learning approaches (Goodfellow et al., 2016) because the available data is too shallow, there is no spatial information, and the number of variables per patient data entry is too small to generate high dimensional hierarchical representations. Additionally, current data enrichment techniques are not able to deal well with categorical variables. There is no precedent literature on the application of deep learning to delirium prediction, contrary to the prediction of readmissions (Artetxe et al., 2018; Artetxe, Ayerdi, et al., 2017; Artetxe, Beristain,

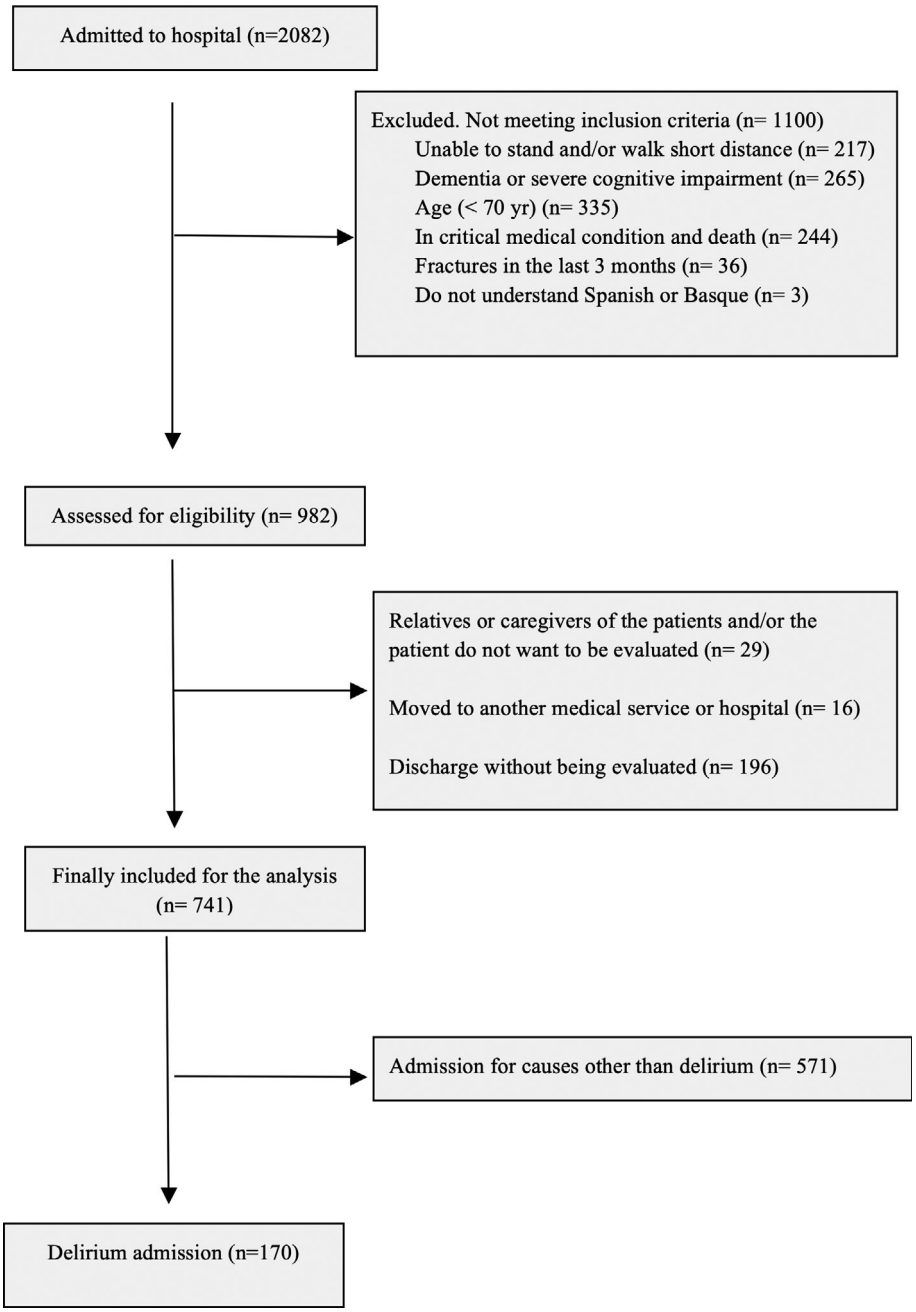

FIGURE 1 Flow diagram of the recruitment process

et al., 2017; Artetxe, Graña, et al., 2017; Garmendia et al., 2017, 2019). Specifically, we have applied the following machine learning classifier building methods:

- K nearest neighbours (k-NN) are the basic non-linear model free case base reasoning approach that often provide the baseline results achieved with the simplest models. The training set is used unprocessed. The class estimation of a test input pattern is given by the majority voting among the classes associated with the K samples from the training dataset which are closest using some specific distance (often the euclidean distance).
- Random forests (RF) are a randomized model that provides top state of the art results in many instances, they can be built very quickly, and they are quite robust to data distribution changes. RF was proposed by Breiman (Breiman, 2001) as an ensemble of classification trees where each tree is trained upon a bootstrapped version of the training dataset and using a random subsets of the data variables for the node split decisions. The class estimation for a test input vector is given by the majority voting over the responses of the ensemble classifiers. The randomization is intended to maximise diversity of the classifiers as a mean to ensure robustness.

TABLE 1 Demographics information of the cohort

Stats		
Gender		
Male	382	51.55%
Female	359	48.45%
Weight		
Mean (SD)	67.43 (13.60)	
Age		
Mean (SD)	84.37 (6.76)	
Marital st.		
Married	265	35.60%
Single	65	1.90%
Divorced	13	8.90%
Widowed	265	35.60%
NA	133	18%
Has children	501	67.61%
Walking help	419	56.54%
Living at		
Own home	530	71.52%
Alone	195	26.31%
Other's home	62	8.36%
Residence	64	8.63%
Pharma		
Oligopharma <5	178	24.02%
Moderate (5–9)	358	48.31%
Severe (>9)	205	27.67%
Admittance reason = delirium	170	22.94%

- Boosting classification (BC) or gradient boosting is an ensemble of weak classifiers, in our case decision trees, that is built incrementally by selecting the weak classifier that points in the negative direction of the gradient of a differentiable loss function (Friedman, 2002).

For the validation and model assessment we apply a hold out approach, where 20% of the sample is used as testing data. The remaining 80% is partitioned into training and validation datasets. We apply a search for the optimal metaparameters (i.e., k in k-NN, number of trees in RF and BC) by selecting the best performing on the validation dataset. We repeat the complete training searching for the optimal model and testing 10 times, reporting the average performance results. A long term goal for the clinical point of view is the construction of computer aided diagnostic systems supporting the clinician in the assessment of the patients. The computational experiments reporting the results of different approaches to predictive model building are useful in this long term endeavour by providing prospective performance assessments. They also provide evidence for the CAD system inclusion in the clinical practice.

3.2 | Variable selection

A major aim of this study is the identification of risk factors for delirium condition at hospital admittance. We achieve this identification by two complementary means. First we compute the univariate logistic regression on each variable, using the resulting p-value as a measure of variable significance in isolation, without taking into account interaction effects. For the multivariate point of view we consider the variable importance computed by the RF and BC approaches as the loss of classification performance due to the removal of this variable.

3.3 | Classification performance metrics

At each validation bootstrapped repetition we compute the confusion matrix and performance metrics derived from it, finally reporting the average of these results. Let us define TP, TN, FP, and FP as true positive, true negative, false positive and false negative counts. We compute the

accuracy $\left(A = \frac{TP+TN}{TP+TN+FP+FN}\right)$, the F1 score $\left(F1 = 2\frac{P \cdot R}{P+R}\right)$, where $P = \frac{TP}{TP+FP}$ and $R = \frac{TP}{TP+FN}$. The analysis using receiver operating characteristic (ROC) is a plot of sensitivity Sens $= \frac{TP}{TP+FN}$ versus the false positive rate $\left(FPR = \frac{FP}{FP+TN}\right)$. It is widely used to compare performances of state of art of supervised learning classification methods. Specifically we report the integral of the ROC, that is, the area under ROC curve (AUC).

4 | RESULTS

Table 2 shows the most significant variables according to a univariate logistic regression, where we have found some demographics like age, weight, and previous admittance in the last 30 days. Frailty scales (Barthel, Fried, MNA, Pfeiffer) are also found significative effects for delirium. Comorbidities such as falls and dementia have strong correlation with delirium. History of pharmacy with neuroleptics and antidepressant medicaments seem to contribute greatly to delirium emergence. The greatest odds ratio (OR) correspond to psychoactive medications Neuroleptics (6.388), Quetiapina (8.597), Haloperidol (24.479), Antipsychotics (3.022), Antidepressants (2.347), Antiespasmodic (2.255), and to neural comorbidities such as Dementia (15.954) and Parkinson (3.182).

Table 3 provides the average classification performance by k-NN, RF and BC of 10 repetitions of the model seeking and test. The AUC for k-NN is significantly lower than RF and BC, otherwise RF and BC are equivalent. Classification performance measured by F1 score is significantly greater for BC (Welch's t test, $p < 0.001$), but accuracy is below 0.8. Finally, Table 4 shows the variables that appear more than five times in the selection of the 10 most important variables according to their effect on classification performance for RF and BC. The Pfeiffer scale is the most important aggregate variable in most of the train and test repetitions. Other variables that are common in both classifiers are the SPPB aggregate and the individual tests, as well as the MNA calf's circumference and previous neuropsychological problems. The use of neuroleptic medicaments is the most important pharmacological variable for delirium prediction.

5 | DISCUSSION

Some sociodemographic variables, such as gender, age and weight, appear as relevant for the early diagnostics of delirium. Age and gender have been recognized as natural immediate factors of delirium onset (Kukreja et al., 2015). Weight may be related to nutritional features discussed below. Specifically, age is a primary relevant factor for delirium, both by univariate logistic regression and in multivariate classification analysis, which is in agreement with the literature (Inouye et al., 2014; Setters & Solberg, 2017).

The patient functional status measured by Barthel scale appears as delirium predictors showing that higher dependency for basic daily living activities conveys greater risk of delirium at hospital admittance (Johnson, 2018). In our analysis patients with better physical capacity according to SPPB scale have lower probability of delirium than those with worse SPPB performance. Similar results have been reported on patients from the surgery areas (Jung et al., 2015). We have found a strong effect of nutritional parameters measured by the MNA scale and the emergence of delirium. There are few studies that relate nutrition as a risk factor for delirium. Most recent ones are focused on patients at intensive care units after traumatic surgery (Jung et al., 2015), showing that malnutrition is predictive factor of delirium in the post-operatory phase (Chu et al., 2016).

Delirium onset depends on a complex relation between basal vulnerability and the severity of the precipitating factors (Inouye & Charpentier, 1996). Highly vulnerable patients can develop into delirium after a small insult, while patients with strong basal state may suffer stronger before developing into delirium state. This vulnerability, also known as frailty, is a geriatric condition characterized by the loss of strength, resilience and physiological functions. Frailty has been related with delirium onset after hospital discharge (Verloo et al., 2016) where nine out of ten patients with delirium were assessed as frail. However, other studies (Joosten et al., 2014) found that frailty is of limited value to predict delirium, though it was predictive of 6 months mortality, while there is evidence that delirium impact on mortality is greater on the fitter subjects (Dani et al., 2017), and that full syndrome delirium (FSD) is a definitive risk factor mortality in acute hospital admittance (Diwell et al., 2018). Conversely, delirium has been postulated as a cognitive harbinger of frailty (Bellelli et al., 2017) because they share multiple pathopsychologic pathways. Therefore, it is no surprise that some of the hallmarks of frailty are relevant risk factors for delirium.

Dementia is another comorbidity and risk factor for delirium found in our study. Patients with worse scores in the Pfeiffer questionnaire cognitive scoring have greater probability of delirium. Delirium superimposed on dementia has been found increasing the mortality in hospitalized older adults (Avelino-Silva et al., 2017). A strong bidirectional relation between delirium and dementia is supported by growing evidence from epidemiological, clinicopathological, neuroimaging, biomarker, and experimental studies (Fong et al., 2015).

Of the potential pharmacological effects for delirium identified in Table 2 by strong significance and large OR, only the neuroleptics are identified by the multivariate classification approach. Patients with dementia associated to behavioural disorders using psychoactive drugs, including neuroleptics (often while living in the community), are more prone to delirium (Morandi et al., 2014). However, the literature shows that the treatment of ACS patients with antipsychotics needs high personalization (Rivière et al., 2019), hence no definitive general conclusion may be given from the results.

TABLE 2 Most significant variables found by univariate logistic regression relative to delirium at the hospital admittance

				Wald test			
Variable	**Est.**	**SE**	***z***	**WS**	**DF**	***p***	**OR**
Age	−0.076	0.014	−5.345	28.564	1	<0.001	0.927
Sex	−0.418	0.176	−2.376	5.646	1	0.017	0.658
R30	0.471	0.222	2.119	4.49	1	0.034	1.602
weight	0.034	0.007	4.690	21.998	1	<0.001	1.034
Functional and frailty scales							
Barthel	0.866	0.128	6.790	46.106	1	<0.001	2.378
Pfeiffer	−1.017	0.100	−10.221	104.460	1	<0.001	0.362
MNA	−0.581	0.128	−4.546	20.664	1	<0.001	0.560
MNA-Mobility	0.833	0.178	4.675	21.859	1	<0.001	2.299
MNA-NP	1.554	0.202	7.691	59.159	1	<0.001	4.731
MNA-CC	0.382	0.064	5.996	35.957	1	<0.001	1.465
Fried	−0.493	0.189	−2.607	6.798	1	0.009	0.610
Fried-Mood	−0.389	0.178	−2.184	4.771	1	0.029	0.677
Fried-March	1.453	0.304	4.775	22.805	1	<0.001	4.275
Fried-PA	0.708	0.179	3.958	15.662	1	<0.001	2.029
SPPB	0.684	0.103	6.627	43.916	1	<0.001	1.982
SPPB-sitting	0.647	0.103	6.282	39.464	1	<0.001	1.909
SPPB-balance	0.396	0.066	6.027	36.321	1	<0.001	1.486
SPPB-March 4 m	0.510	0.097	5.244	27.495	1	<0.001	1.666
Comorbidities							
hearing loss	0.524	0.177	2.961	8.769	1	0.003	1.688
falls	0.926	0.183	5.060	25.604	1	<0.001	2.525
disfagia	0.610	0.259	2.359	5.564	1	0.018	1.841
Cho/DL	−0.458	0.191	−2.401	5.763	1	0.016	0.632
TCE	0.684	0.294	2.328	5.418	1	0.020	1.981
ICC	−0.517	0.210	−2.456	6.032	1	0.014	0.596
Dementia	2.770	0.506	5.473	29.955	1	<0.001	15.954
Parkinson	1.157	0.446	2.595	6.734	1	0.009	3.182
Glaucoma	−1.060	0.408	−2.597	6.742	1	0.009	0.346
AHT	−0.448	0.189	−2.374	5.636	1	0.018	0.639
Pharmacology							
Hypnotic	0.403	0.180	2.234	4.989	1	0.026	1.496
Benzodiazapina (BZN)	0.437	0.182	2.397	5.746	1	0.017	1.548
Neuroleptics	1.854	0.301	6.171	38.081	1	<0.001	6.388
Quetiapina	2.151	0.540	3.985	15.883	1	<0.001	8.597
Haloperidol	3.198	1.073	2.981	8.886	1	0.003	24.479
Antipsychotics-other	1.106	0.525	2.106	4.436	1	0.035	3.022
Antidepressants	0.853	0.196	4.353	18.950	1	<0.001	2.347
Mod. lipids	−0.497	0.188	−2.648	7.011	1	0.008	0.608
Antiespasmodic	0.813	0.397	2.046	4.187	1	0.041	2.255
Laxatives	0.794	0.314	2.532	6.410	1	0.011	2.213

Abbreviations: AHT, arterial hypertension; DF, degrees of freedom; MNA-NP, neuropsychological problems; OR, odds ratio; PA, physical activity; R30, readmission <30 days; SE, standard error; WS, Wald statistic; z, *z* score.

TABLE 3 Classification performance results averaged over 10 repetitions of hold-out training, validation and testing

	A	AUC	F1
k-NN	0.765	0.597	0.705
RF	0.770	0.745	0.718
BC	0.798	0.743	0.755

TABLE 4 Variable importance identified by RF and BC measured as the number of times (NT) that the variable appears in the 10 top in the validation and testing repetitions

RF		BC	
Variable	**NT**	**Variable**	**NT**
Pfeiffer	9	Pfeiffer	10
SPPB-sit	8	MNA-NP	10
MNA-NP	8	Neuroleptics	8
Neuroleptics	7	MNA-CC	7
SPPB	7	Age	7
SPPB-bal	6	SPPB-sit	7
Dementia	6	weight	7
SPPB-w	6	MNA	6
MNA-CC	5	MNA-WL3m	6
Age	5	SPPB	6
FRIED-PA	5	R30	5
MNA	5	MNA-m	5
AH	5	SPPB-bal	5
		Dementia	5

Abbreviations: AH, antidepressant heterocyclic; FRIED-PA, physical activity; MNA-CC, calf circumference; MNA-m, mobility; MNA-NP, neuropsychological problems; MNA-WL3m, weight loss 3 months; R30, readmission <30 days; SPPB-bal: balance test; SPPB-sit, sitting; SPPB-w: walking 4 m.

5.1 | Limitations

As a multifactorial disease, delirium risk factors identification in a cohort is heavily dependent on its demographics and prevalent conditions. As our cohort does not contain some conditions, such as alcohol abuse, they are not detected though they are reported in the literature (Setters & Solberg, 2017). Another limitation is the cohort has been recruited in a single site. Multisite extensions of the study will be welcomed to confirm some of the conclusions.

6 | CONCLUSIONS AND FUTURE WORK

Delirium is a highly prevalent syndrome in hospitalized older patients which worsens their prognostic. This paper explores the construction of machine learning based predictors based on an ample set of demographic, clinical, and pharmacological variables. Classification performance results are encouraging. Further exploration of machine learning methods such as multitask learning may improve them, but at the present level it is possible to use the variable importance provided by the classifiers to identify the most salient risk factors for delirium in the population represented by our dataset. We have found a strong association with frailty and dementia indices. Also, we have found strong pharmacological risks, specially the use of neuroleptics. Future work should be addressed to increase the data base for the experimentation and to build an extensive inter site dataset, at international level if possible.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

ENDNOTE

[1] https://jasp-stats.org.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

Aboderin, I. A. G., & Beard, J. R. (2015). Older people's health in sub-saharan africa. *The Lancet*, *385*, e9–e11. https://doi.org/10.1016/S0140-6736(14)61602-0

Artetxe, A., Ayerdi, B., Graña, M., & Rios, S. (2017). Using anticipative hybrid extreme rotation forest to predict emergency service readmission risk. *Journal of Computational Science*, *20*, 154–161.

Artetxe, A., Beristain, A., & Graña, M. (2018). Predictive models for hospital readmission risk: A systematic review of methods. *Computer Methods and Programs in Biomedicine*, *164*, 49–64. https://doi.org/10.1016/j.cmpb.2018.06.006

Artetxe, A., Beristain, A., Graña, M., & Besga, A. (2017). Predicting 30-day emergency readmission risk. In M. Graña, J. M. López-Guede, O. Etxaniz, Á. Herrero, H. Quintián, & E. Corchado (Eds.), *International joint conference SOCO'16-CISIS'16-ICEUTE'16* (pp. 3–12). Springer International Publishing.

Artetxe, A., Graña, M., Beristain, A., & Ríos, S. (2017). Balanced training of a hybrid ensemble method for imbalanced datasets: A case of emergency department readmission prediction. *Neural Computing and Applications*, *32*(10), 5735–5744.

Avelino-Silva, T. J., Campora, F., Curiati, J. A. E., & Jacob-Filho, W. (2017). Association between delirium superimposed on dementia and mortality in hospitalized older adults: A prospective cohort study. *PLoS Medicine*, *14*, e1002264.

Bellelli, G., Moresco, R., Panina-Bordignon, P., Arosio, B., Gelfi, C., Morandi, A., & Cesari, M. (2017). Is delirium the cognitive harbinger of frailty in older adults? A review about the existing evidence. *Frontiers in Medicine*, *4*, 188. https://doi.org/10.3389/fmed.2017.00188

Besga, A., Ayerdi, B., Alcalde, G., Manzano, A., Lopetegui, P., Graña, M., & González-Pinto, A. (2015). Risk factors for emergency department short time readmission in stratified population. *BioMed Research International*, *2015*, 685067.

Breiman, L. (2001). Random forest. *Machine Learning*, *45*, 5–32.

Charlson, M. E., Pompei, P., Ales, K. L., & MacKenzie, C. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Diseases*, *40*, 373–383. https://doi.org/10.1016/0021-9681(87)90171-8

Chu, C.-S., Liang, C.-K., Chou, M.-Y., Lin, Y.-T., Hsu, C.-J., Chou, P.-H., & Chu, C.-L. (2016). Short-form mini nutritional assessment as a useful method of predicting the development of postoperative delirium in elderly patients undergoing orthopedic surgery. *General Hospital Psychiatry*, *38*, 15–20.

Dani, M., Owen, L. H., Jackson, T. A., Rockwood, K., Sampson, E. L., & Davis, D. (2017). Delirium, frailty, and mortality: Interactions in a prospective study of hospitalized older people. *The Journals of Gerontology: Series A*, *73*, 415–418. https://doi.org/10.1093/gerona/glx214

Diwell, R. A., Davis, D. H., Vickerstaff, V., & Sampson, E. L. (2018). Key components of the delirium syndrome and mortality: Greater impact of acute change and disorganised thinking in a prospective cohort study. *BMC Geriatrics*, *18*, 24.

Erkinjuntti, T., Sulkava, R., Wikström, J., & Autio, L. (1987). Short portable mental status questionnaire as a screening test for dementia and delirium among the elderly. *Journal of the American Geriatrics Society*, *35*, 412–416. https://doi.org/10.1111/j.1532-5415.1987.tb04662.x

Feldman, J., Yaretzky, A., Kaizimov, N., Alterman, P., & Vigder, C. (1999). Delirium in an acute geriatric unit: Clinical aspects. *Archives of Gerontology and Geriatrics*, *28*, 37–44.

Ferrucci, L., Guralnik, J. M., Salive, M. E., Fried, L. P., Bandeen-Roche, K., Brock, D. B., Simonsick, E. M., Corti, M., & Zeger, S. L. (1996). Effect of age and severity of disability on short-term variation in walking speed: The women's health and aging study. *Journal of Clinical Epidemiology*, *49*, 1089–1096. https://doi.org/10.1016/0895-4356(96)00231-4

Fong, T. G., Davis, D., Growdon, M. E., Albuquerque, A., & Inouye, S. K. (2015). The interface between delirium and dementia in elderly adults. *Lancet Neurology*, *14*, 823–832.

Fried, L., Tangen, C., Walston, J., Newman, A., Hirsch, C., Gottdiener, J., Seeman, T., Tracy, R., Kop, W., Burke, G., & McBurnie, M. (2001). Frailty in older adults: Evidence for a phenotype. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, *56*, M146–M156.

Friedman, J. H. (2002). Stochastic gradient boosting: Nonlinear methods and data mining. *Computational Statistics & Data Analysis*, *38*, 367–378. https://doi.org/10.1016/S0167-9473(01)00065-2

Garmendia, A., Graña, M., Lopez Guede, J., & Rios, S. (2019). Neural and statistical predictors for time to readmission in emergency departments: A case study. *Neurocomputing*, *354*, 3–9.

Garmendia, A., Graña, M., Lopez-Guede, J. M., & Rios, S. (2017). Predicting patient hospitalization after emergency readmission. *Cybernetics and Systems*, *48*, 182–192. https://doi.org/10.1080/01969722.2016.1276772

Goodfellow, I., Bengio, Y., & Courville, A. (2016). *Deep learning*. MIT Press.

Gower, L. E. J., Gatewood, M. O., & Kang, C. S. (2012). Emergency department management of delirium in the elderly. *The Western Journal of Emergency Medicine*, *13*, 194–201.

Guralnik, J. M., Simonsick, E. M., Ferrucci, L., Glynn, R. J., Berkman, L. F., Blazer, D. G., Scherr, P. A., & Wallace, R. B. (1994). A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission. *Journal of Gerontology*, *49*, M85–M94. https://doi.org/10.1093/geronj/49.2.M85

Haykin, S. (1998). *Neural networks: A comprehensive foundation*. Prentice-Hall.

Inouye, S. K., & Charpentier, P. A. (1996). Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. *JAMA*, *275*, 852–857.

Inouye, S. K., Westendorp, R. G. J., & Saczynski, J. S. (2014). Delirium in elderly people. *The Lancet*, *383*, 911–922.
Johnson, J. R. (2018). Delirium in hospitalized older adults. *The New England Journal of Medicine*, *378*, 96.
Joosten, E., Demuynck, M., Detroyer, E., & Milisen, K. (2014). Prevalence of frailty and its ability to predict in hospital delirium, falls, and 6-month mortality in hospitalized older patients. *BMC Geriatrics*, *14*(1). https://doi.org/10.1186/1471-2318-14-1
Jung, P., Pereira, M. A., Hiebert, B., Song, X., Rockwood, K., Tangri, N., & Arora, R. C. (2015). The impact of frailty on postoperative delirium in cardiac surgery patients. *The Journal of Thoracic and Cardiovascular Surgery*, *149*, 869–875.
Kaiser, M. J., Bauer, J. M., Ramsch, C., Uter, W., Guigoz, Y., Cederholm, T., Thomas, D. R., Anthony, P., Charlton, K. E., Maggio, M., Tsai, A. C., Grathwohl, D., Vellas, B., Sieber, C. C., & MNA-International Group. (2009). Validation of the mini nutritional assessment short-form (mna-sf): A practical tool for identification of nutritional status. *The Journal of Nutrition, Health and Aging*, *13*, 782. https://doi.org/10.1007/s12603-009-0214-7
Kuhn, M., & Johnson, K. (2013). *Applied predictive modeling*. Springer.
Kukreja, D., Günther, U., & Popp, J. (2015). Delirium in the elderly: Current problems with increasing geriatric age. *The Indian Journal of Medical Research*, *142*, 655–662.
Lipowski, Z. J. (1987). Delirium (acute confusional states). *JAMA*, *258*, 1789–1792.
Magny, E., Le Petitcorps, H., Pociumban, M., Bouksani-Kacher, Z., Pautas, É., Belmin, J., Bastuji-Garin, S., & Lafuente-Lafuente, C. (2018). Predisposing and precipitating factors for delirium in community-dwelling older adults admitted to hospital with this condition: A prospective case series. *PLoS One*, *13*, e0193034.
Mahoney, F. I., & Barthel, D. W. (1965). Functional evaluation: The barthel index. *Maryland State Medical Journal*, *14*, 61–65.
Morandi, A., Davis, D., Fick, D. M., Turco, R., Boustani, M., Lucchi, E., Guerini, F., Morghen, S., Torpilliesi, T., Gentile, S., MacLullich, A. M., Trabucchi, M., & Bellelli, G. (2014). Delirium superimposed on dementia strongly predicts worse outcomes in older rehabilitation inpatients. *Journal of the American Medical Directors Association*, *15*, 349–354.
Ohl, I. C. B., Chavaglia, S. R. R., Ohl, R. I. B., Lopes, M. C. B. T., Campanharo, C. R. V., Okuno, M. F. P., & Batista, R. E. A. (2019). Evaluation of delirium in aged patients assisted at emergency hospital service. *Revista Brasileira de Enfermagem*, *72*, 153–160.
Pfeiffer, E. (1975). A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *Journal of the American Geriatrics Society*, *23*, 433–441.
Rivière, J., van der Mast, R. C., Vandenberghe, J., & Van Den Eede, F. (2019). Efficacy and tolerability of atypical antipsychotics in the treatment of delirium: A systematic review of the literature. *Psychosomatics*, *60*, 18–26.
Rodriguez-Mañas, L., & Fried, L. P. (2015). Frailty in the clinical scenario. *The Lancet*, *385*, e7–e9. https://doi.org/10.1016/S0140-6736(14)61595-6
Setters, B., & Solberg, L. M. (2017). Delirium. *Primary Care*, *44*, 541–559.
Sourial, N., Bergman, H., Karunananthan, S., Wolfson, C., Payette, H., Gutierrez-Robledo, L. M., Béland, F., Fletcher, J. D., & Guralnik, J. (2013). Implementing frailty into clinical practice: A cautionary tale. *The Journals of Gerontology: Series A*, *68*, 1505–1511. https://doi.org/10.1093/gerona/glt053
Vaughan, L., Corbin, A., & Goveas, J. (2015). Depression and frailty in later life: A systematic review. *Clinical Interventions in Aging*, *10*, 1947–1958.
Vellas, B., Guigoz, Y., Garry, P. J., Nourhashemi, F., Bennahum, D., Lauque, S., & Albarede, J. L. (1999). The mini nutritional assessment (mna) and its use in grading the nutritional state of elderly patients. *Nutrition*, *15*, 116–122.
Verloo, H., Goulet, C., Morin, D., & von Gunten, A. (2016). Association between frailty and delirium in older adult patients discharged from hospital. *Clinical Interventions in Aging*, *11*, 55–63.
Witten, I. H., Frank, E., & Hall, M. A. (2011). *Data mining: Practical machine learning tools and techniques* (3rd ed.). Morgan Kaufmann Publishers Inc.

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APPENDIX: DESCRIPTION OF THE VARIABLES

- Age integer valued.
- Sex: Binary valued, encoded "1" for male "2" for female.
- Fried: The fried phenotype method considers weight loss, exhaustion, physical activity level, grip strength, and walking speed, functional capacity. This method classifies older adults as frail, pre-frail or non-frail based on five criteria. Frail participants scored below the cut-offs for three or more criteria, pre-frail participants scored below the cut-offs for one or two criteria, and non-frail participants did not score below the cut-offs for any criteria (Fried et al., 2001). Categorical valued: (0 = robust, 1–3: pre-frail, ≥3: frail).
- SPVV: the survival probability coefficient corresponding to the comorbidity measured with the Charlson Comorbidity Index (CCI) (Charlson et al., 1987) describing 19 conditions and assigning a score of 1 to 6 depending on the associated risk of dying.
- SPPB: The Short Physical Performance Battery (SPPB), combines balance, gait velocity, and leg strength as a single score on a 0 (worst) to 12 (best scale). Consists of three assessments: (1) repeated chair stands (sit); (2) balance tests (bal) (side-by-side, semitandem and tandem balance tests); (3) an eight-foot walk test. In order to classify participants as frail, pre-frail and non-frail, the following cut-offs were used: SPPB 0–6 (frail), SPPB 7–9 (pre-frail), SPPB 10–12 (non-frail) (Guralnik et al., 1994).
- MNA: Nutrition was assessed with the mini Nutritional Assessment (MNA) short form (Kaiser et al., 2009), consisting of six questions scored from zero to two or three. These questions address recent weight loss, appetite loss, mobility, psychological stress, neuropsychological problems, and body mass index (BMI). A total score above 12 points is considered "normal—not at risk," a score between 8 and 11 points is considered "possible malnutrition" and below 8 points "malnutrition."
- Falls: The number of falls in the previous 6 months. Integer positive valued.
- March: the scoring achieved in the SPPB test in the walk test. Integer valued.
- Mobility: degrees of mobility from none (staying at bed) to outdoors independent mobility. Categorical values {1,2,3}.
- Number of drugs prescribed at the time of discharge. Integer valued.
- Neuro: the degree of neuropsychological disorders in the 6 months previous to admission from non existent to very strong. Categorical values {1,2,3}. Part of MNA test.
- Weight-loss (WL3m): loss of weight in the previous 3 months, Boolean valued encoded {0,1}. Part of MNA test.
- Weakness: increased weakness previous to admission. Boolean valued encoded {0,1}.
- Pfeiffer: Pfeiffer's Short Portable Mental Status Questionnaire (SPMSQ) is a brief screening test for organic brain syndromes(Erkinjuntti et al., 1987). Score integer valued {0,1,...,10}.
- Acute sickness in the 3 months previous to admission. Boolean valued encoded {0,1}.
- R30: the patient admission is a readmission after less than 30 days.