Association between Cognitive Status before Surgery and Outcomes in Elderly Patients with Hip Fracture in a Dedicated Orthogeriatric Care Pathway

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<u>**Running title:**</u> Dementia and prognosis of hip fracture

1

Abstract (word count: 250)

Background: Dementia is associated with a worse prognosis of hip fracture, but the impact of a dedicated geriatric care pathway on the prognosis of these patients has not been evaluated.

Objective: According to the cognitive status before surgery, our main objective was to compare mortality rate at 6 months; secondary outcomes were to compare in-hospital complications, the risk of new institutionalization and the ability to walk at 6 months.

Methods: Between 2009 and 2015, all patients (> 70 years) admitted after hip fracture surgery into a dedicated unit of peri-operative geriatric care were included: patients with dementia (DP), without dementia (NDP) and with cognitive status not determined (CSND). Data are expressed as Hazard Ratio(HR) for multivariate cox analysis or Odds Ratio(OR) for multivariate logistic regression analysis and their 95% confidence interval (CI).

Results: We included 650 patients (86 ± 6 years): 168 DP, 400 NDP and 82 CSND. After adjustment for age, sex, comorbidities, polypharmacy, pre-fracture autonomy, time-to-surgery and delirium, there were no significant differences for 6-month mortality (DP vs NDP: HR=0.7[0.4 − 1.2], DP vs CSND: HR=0.6[0.3 − 1.4], CSND vs NDP: HR=0.8[0.4 − 1.7]); but DP and CSND were more likely to be newly institutionalized after 6 months compared to NDP (OR DP=2.6[1.4 − 4.9], p=0.003, OR CSND=2.9[1.4 − 6.1], p=0.004). 92% of population was walking after 6 months (63% with assistance): no difference was found between the 3 groups.

Conclusion: In a dedicated geriatric care pathway, DP and CSND undergoing hip surgery have the same 6-month mortality and walking ability as NDP.

Key words: Unit of Peri-Operative Geriatric care, Hip fracture, Dementia, Elderly

1. Introduction

As a consequence of the aging of the population, the incidence of osteoporotic fractures, especially hip fractures (HF), is increasing [1,2]. In 2000, the worldwide incidence of HF was estimated at 1.6 million in people aged 50 years and older [1]. The annual global incidence of HF is expected to rise to between 7.3 and 21.3 million by the year 2050 [3]. Nearly all HF occur as a result of a fall and many fall again soon after sustaining the fracture [4]. Direct medical costs incurred are staggering, estimated at between US \$153.5 billion and US \$446.3 billion annually by 2050 [5]. The rate of death is high, varying from 12 to 23% during the 6 months following the fracture, higher than in the general population in the following months and years [6,7].

Dementia affects 36 million people worldwide, with numbers expected to double every 20 years to 66 million by 2030 [8]. Among dementia, notably in the geriatric population, Alzheimer's disease (AD) is the most frequent neurodegenerative disorder [9], but cognitive impairment remains under diagnosed [8]. In 2009, Sampson et al. showed that 42% of unselected older medical inpatients had dementia, half of these had not previously been diagnosed with dementia[10].

AD and HF are closely related [11]. Baker and al. found that patients with AD had a 3.2 hazard ratio for risk of HF (95% CI, 2.4 – 4.2) compared to non-AD patients, after controlling for potential confounders [12]. In their study, the incidence of HF among patients with and without AD was 17.4 (95% CI, 15.7–19.2) and 6.6 (95% CI, 5.8–7.6) per 1,000 person years, respectively [12]. In particular, mortality and poor functional recovery after HF seem to be more frequent in patients with dementia than in patients without dementia [12-15]. Among the patients who experienced a HF, 24 to 27% of patients with dementia and 10 to 14% of patients without dementia did not survive more than six months after the occurrence of a HF [7,12].

Because most of HF occur in older patients, the prevalence of comorbid conditions and frailty is high among this population [16,17]. They are at high risk of developing complications such as delirium, infection and drug related problems. Recently, there has been an increasing interest for the development of collaborations between orthopedic surgeons, anesthesiologists and geriatricians. Hospitals and health systems have implemented ortho-geriatric care to improve patient outcomes, with conflicting results [2,4,18-25].

In a previous study [26], we demonstrated that early admission to a dedicated geriatric unit improved 6-month mortality and morbidity in elderly patients with HF. Our study did not focus on patients with dementia (38% of our population). However, the question of the benefit of a dedicated geriatric unit post HF in patients with dementia is still unexplored.

Our hypothesis was that, whatever the cognitive status before surgery, all patients admitted with hip fracture in an orthogeriatric-dedicated care pathway, with staff trained to manage patients with dementia, would have the same prognosis at 6 months. Our main objective was to compare mortality rate at 6 months regarding the cognitive status before surgery. Secondary outcomes were to compare: in-hospital complications, including delirium; the risk of new institutionalization and the ability to walk at 6 months, according to the cognitive status before surgery.

2. Materials and Methods

This study was approved by the hospital ethics committee (CPP Ile de France VI, Paris, France), and informed consent was waived, as the study was observational. The database was declared to the French National Commission on Computing and Liberty (CNIL, Paris, France).

2.1 Study population

From July 2009 to December 2015, all patients admitted to our emergency department (ED) were evaluated for eligibility. Detailed methodology including the opening of a new geriatric unit (UPOG: Unit for Peri-Operative Geriatric care) has been previously reported [26], and some of these patients were included in previous studies [26,27]. Patients were included if their primary admission was due to HF and if they were aged over 70. Patients were not included if they were admitted with multiple fractures, a metastatic fracture or a fracture complicated by a previous hip prosthesis or osteosynthesis.

Their cognitive status before surgery was obtained from the patients themselves, family members, caregivers and from their general practitioners who were systematically contacted (phone call), and determined as follows:

1- Patients with dementia (DP): with a previous diagnosis of dementia by a geriatrician or a neurologist using internationally recognized criteria and DSM-IV criteria [8-10,28]. These patients had had a cognitive screening with a neuropsychologist using screening instruments and a cerebral imaging. Some of them were treated by specific treatments (anticholinesterase inhibitors or antiglutamate) that only neurologists, psychiatrists and geriatricians are authorized to prescribe in France.

2- Patients without dementia (NDP): with no known previous cognitive impairment, without memory or cognitive complaint before admission to our hospital (according to family and to general practitioner), without specific treatment and still complaint-free at 6 months. Because

they were not included in DSM-IV criteria that defined dementia, it is to note that these patients did not have a complete cognitive assessment with a neuropsychologist before or after the hospitalization.

3- Patients with cognitive status not determined (CSND): with a history of previous cognitive impairment without cognitive evaluation or conclusive cognitive evaluation (unexplored or unlabeled). As detailed in the introduction, there are a significant proportion of patients under diagnosed [8,10]. In this group, patients possibly had dementia, mild cognitive impairment (MCI) or other conditions with cognitive consequences. Without an accurate diagnosis, we have chosen to create this third group of patients.

2.2 Design study

The data were prospectively entered in the database, including age, sex, own home or nursing home, living conditions, walking ability, medical history, type of fracture and surgical treatment, time-to-surgery (delay) and duration of surgery. Co-morbidity severity was assessed using the Cumulative Illness Rating Scale (CIRS-G) [29] in which co-occurring medical conditions are weighted from 0 to 4 in 13 main systems. Pre-hospitalization functional status was assessed using the Activities of Daily Living (ADL) scale[30]. We recorded preoperative hemoglobin level and its lowest value during the hospitalization, serum creatinine and estimated creatinine clearance using the Cockcroft formulae. All complications during the hospitalization were recorded, including delirium using the Confusion Assessment Method scale [31] (assessment on arrival and then once a day consistently), use of physical restraints, stool impaction, urinary retention requiring drainage, morphine administration, pressure ulcer, infection, phlebitis or pulmonary embolism, blood transfusion, cardiac insufficiency (*i.e.* acute cardiac failure or acute pulmonary edema), and admission into an intensive care unit (ICU). To prevent and manage the occurrence of possible delirium, we used the recommendations proposed by Inouye et al. (non-pharmacological and

6

pharmacological acute treatment strategies) [31,32]. Management strategy focused on early mobilization with the aim of chair-sitting and walking (first steps) within 24 and 48 hours. Patients were studied until death or 6 months after admission, for survival, walking ability (outdoors, with or without assistance) and new institutionalization. Surviving patients or their relatives were evaluated in the usual ambulatory clinic assessment, or contacted and interviewed by telephone; ADL scale and MMSE (Mini-Mental State Examination) were usually done [8,10]. Missing patients were tracked through health care providers, particularly general practitioners, or any identified acquaintances. The primary endpoint was 6-month mortality and secondary endpoints were i) 6-month functional outcome including new institutionalization and ability to walk ii) postoperative complications including delirium. Our study compared the 3 groups of patients, in pairs: patients with dementia (DP), patients without dementia (NDP) and patients with cognitive status not determined (CSND).

2.3 Statistical analysis

Data are presented as mean ± SD, median [25–75 interquartile] for non-Gaussian variables, or number (percentages). Comparisons between 3 groups were performed using a Kruskal Wallis test for quantitative variables, followed by a Dunn test when a significant difference was found; and Fisher's exact method for qualitative variables. Survival and the risk of a new institutionalization in the 3 groups of patients were estimated by a multivariate logistic regression analysis and for survival by the Kaplan-Meier method too (differences were assessed by the log-rank test) adjusted for the factors known in the published literature [6,12-15,19,26,33,34] (semi-parsimonious method): age (< 80,81-85, 86-90, > 90), sex (female as reference), comorbidities (CIRS-G, ≤ or > 8) [29], number of drugs per day (< or ≥ 5), pre-fracture ADL6 (≤ 5 or = 6) [30], the ability to walk without assistance before surgery, time-to-surgery (≤ or > 48 hours) and the occurrence of delirium during hospitalization. We tested the association of survival / new institutionalization and cognitive status before surgery in UPOG

7

by calculating the odds ratio (OR) or Hazard ratio (HR) and their 95 percent confidence interval (CI) with these prognostic variables. There was 11 missing data (lost of follow-up) for death at 6 months and new institutionalization at 6 months; we excluded these patients from the main analysis (1,7%).

To assess the weight of dementia in some intra-hospital complications (delirium), admission to rehabilitation care after hospitalization, a multivariate logistic regression analysis was performed and adjusted for the same factors. All P values were two-sided and P < 0.05 was considered significant. R software 3.3.1 was used for statistical analyses (www.cran.r-project.org last date accessed August 10, 2016).

3. Results

3.1 *Characteristics of the population and the 3 groups of patients before HF*

Among the 711 patients with HF admitted to the ED, 650 were included (mean age 86 ± 6 years; 495 (76%) female, median CIRS-G: 9[6 – 12]): 168 patients with dementia (DP: 26%), 400 patients without dementia (NDP: 61%) and 82 with cognitive status not determined (CSND: 13%) (**Figure 1**).

Cardiovascular comorbidities were more prevalent (**Table 1**), 97% of patients previously walked, with assistance in 51% of cases (cane, walking frame, human assistance). Baseline characteristics are presented in **Table 1**.

Among patients with a previous diagnosis of dementia, 59% (n = 99) of them had a diagnosis of Alzheimer's disease, 9% (n = 15) of them had a diagnosis of vascular dementia, 17% (n = 28) of them had a diagnosis of Alzheimer's disease and vascular dementia, 7% (n = 11) of them had a diagnosis of dementia associated with Parkinson's disease, 8% (n = 13) of them had a Lewy body disease, 1 patients suffered from corticobasal degeneration and 1 from multisystem atrophy.

8

Among CSND patients, 20% of them (n = 19) had a cognitive assessment before HF without a diagnosis. Reported by family and / or the general practitioner and / or the patient, memory complaint was the main symptom in 68% (n = 56) of cases, behavioral disorders (aggressiveness or apathy) in 5% (n = 4) of cases, and both in 27% (n = 22) of cases.

DP and CSND patients differed from NDP patients (**table 1**): they were older, had more comorbidities and were less autonomous : they had a pre-fracture ADL 6 lower than NDP patients, they were more often institutionalized, and, when they lived at home, DP patients needed more assistance. In the same way, CSND patients differed from DP patients (**table 1**): they were older, they had a pre-fracture ADL6 higher than DP patients, they were less often institutionalized and, when they lived at home, they needed less often assistance. DP patients were more at risk of repeated falls. There was no significant difference between the 3 groups considering care (type of surgery, time to surgery, time to the UPOG, duration of surgery).

3.2 *Hospitalization: complications and discharge*

Other post-operative complications are described in **Table 2**. During hospitalization, 39% of patients suffered from delirium. Delirium appeared more often in DP (n = 99, 59%) and CSND (n = 50, 61%) patients than in NDP patients (n = 105, 26%), without difference between DP and CSND patients. DP patients had a OR that was 3.12 (95% CI[1.97 – 4.96]) times higher that NDP patients; CSND patients had a OR that was 3.30 (95% CI[1.87 – 5.80]) times higher that NDP patients (p < 0.001) after controlling for potential confounders (**table 3**).

At discharge from the hospital, they were no difference in walking (few steps) between the 3 groups, but DP patients less frequently benefited from rehabilitation stay than NDP and CSND patients (respectively: 67%, 84%, 80%). Nevertheless, after controlling for potential confounders (**table 3**), no difference was found between the 3 groups.

9

3.3 Mortality rate at 6 month

At 6 month, 15% of patients were dead (**table 2).** In univariate analysis, no difference was found between DP/NDP patients (16% vs 14%) and CSND/DP patients (22% vs 16%) for the 6-months mortality rate. There was a significant difference between CSND patients (22%) and NDP patients (14%) (**Table 2**). After controlling for potential confounders (multivariate logistic regression analysis and cox regression analysis), no difference was found (**Table 3, Figure 2, Appendix 1-2-3**): DP vs NDP patients (HR=0.67 95% CI [0.38 – 1.20], p=0.19), DP vs CSND patients (HR=0.65 95% CI [0.28 – 1.45], p=0.29), CSND vs NDP patients (HR=0.84 95% CI [0.41 – 1.68], p=0.62).

3.4 Functional outcomes at 6 month (walk and new institutionalization)

Considering functional outcome, 92% of the patients were walking after 6 months (63% with assistance). No difference was found between 3 groups for walking with assistance: 64% of NDP, 61% of DP and 62% of CSND patients (**Table 2**).

No difference was found between CSND and DP patients for new institutionalization at 6 months in univariate analysis (23% vs 19%). In contrary, DP patients were more frequently newly institutionalized than NDP patients at 6 months (19% vs 8%), as CSND patients compared to NDP patients at 6 months (23% vs 8%) (**Table 2**). After controlling for potential confounders (multivariate logistic regression analysis, **Table 3),** the difference still remains for DP patients vs NDP patients (OR=2.56 95% CI [1.36 – 4.86], p=0.003) and CSND patients vs NDP patients (OR=2.91 95% CI [1.37 – 6.07], p=0.004).

DP and CSND patients had lower ADL score at 6 months that NDP patients (respectively 2[1 – 4], 3[2 – 5] and 5[3 – 6]), and the difference was also significant between CSND and DP patients (**table 2**).

At 6 month, 17% of CSND patients (14 patients) had had a neurocognitive assessment with a diagnosis of Alzheimer's diseases (n=4), vascular dementia (n=3), Alzheimer's disease and

vascular dementia (n=1), Lewy body disease (n=1), supranuclear paralysis (n=2), and 2 without a diagnosis. Considering patients without cognitive assessment, 17 had a MMSE score < 11, 15 a MMSE score > 25, 5 patients did not speak french, 3 refused any assessment. For 28 patients, we did not have cognitive data at 6 months.

4. Discussion

To our knowledge, this is the first study considering the association between cognitive status before surgery and mortality and functional outcomes when geriatricians, together with other specialists in an orthogeriatric dedicated care pathway, manage patients with HF. Interestingly, and despite a higher risk of new institutionalization for patients with dementia and cognitive status not determined, we report a lack of significant difference in 6-month mortality and walking ability between the 3 groups of patients (DP, NDP and CSND).

4.1 Outcomes

These results differ from the published literature in the field where mortality and functional recovery after HF in patients with dementia appear to be worse compared to patients without dementia [12-15] and where patients with dementia benefited less often from rehabilitation services, whose role in the recovery of autonomy and mobility has been repeatedly demonstrated [35,36]. In our population, the mortality rate at 6 months in patients with dementia (16%) or patients with cognitive status not determined (22%) was lower that the rate reported in the literature (24 to 27%) [7,12].

These results suggest, in agreement with other published studies investigating the role of an orthogeriatric assessment [4,18-25], that the management of elderly people with HF should systematically consider a geriatric expertise. Indeed, (1) the management of multimorbidity and frailty in the elderly; (2) a quick surgery and an appropriate anesthesia protocol for the elderly; (3) a prevention of common post-operative complications such as delirium; (4) an

assessment of the risk-benefit ratio of treatments (especially analgesics); (5) a management strategy focused on early mobilization with the aim of chair-sitting and walking (first steps) within 24 and 48 hours and (6) an access for all patients (whatever their cognitive status) to rehabilitation care, are all necessary conditions in a dedicated orthogeriatric unit for a reduction of mortality and the resumption of a rapid autonomy, especially for patients with dementia.

To prevent and manage the occurrence of possible delirium (avoidable with a 30 % risk reduction when using a specialized geriatric intervention [32,37,38]), we used the recommendations proposed by Inouye et al [31,32] every day of hospitalization. Delirium is common after hip fracture surgery (occurring in 35% to 65% of patients) [37], frequently associated with preexisting cognitive impairment and it is predictive of functional decline, institutionalization, and mortality [33,37]: each day of delirium increased the risk of death within 6 months by 17% [34].

We show that dementia was not associated with the time-to-surgery (delay), suggesting that all actors of the perioperative period, particularly emergency physicians, orthopedic surgeons and anesthetists, managed these patients with the same accuracy.

Despite good results for mortality rate at 6 months and a lack of difference in 6-month walking ability (after taking into account their pre-existing conditions), DP and CSND patients were significantly more prone to new institutionalization compared to NDP patients. One of the main risk factors in our multivariate logistic regression was pre-fracture walking ability: patients who needed assistance to walk before surgery (more common in patients with dementia) had 2 times more likely to be newly institutionalized than the others. Despite an early geriatric intervention, HF remains a serious condition that precipitates time to institutionalization and this is probably ahead of the fracture time that we can act to prevent future loss of autonomy.

Although this study cannot conclude to a causal link, our results suggests that an early implementation of a geriatric expertise in the management of hip fractured patients leads to dementia becoming comorbidity among others, and no longer a particularly serious comorbidity.

4.2 Why we choose to create the group "CSND patients":

We deliberately chose to create a group of CSND patients in order to be able to make effective comparisons because according to published literature, cognitive impairment remains under diagnosed [10], and because the situation of undetermined cognitive status of patients in perioperative care is frequent. CSND patients, with no diagnosis of dementia, would have been ranked among the patients without dementia and so, we would have been wrong to compare these two populations (potential differences would have been reduced). Indeed, despite missing data, this group was closer to DP patients (than NDP patients) since 17% of these patients had a diagnosis of dementia, and 20% of them were too severe to be explored according to MMSE score at 6 months. However, they were less often institutionalized before HF, probably due to a lack of medical care for a cognitive diagnosis that was not previously considered, or because they had less severe cognitive deterioration. Finally, CSND group was a heterogeneous group with patients with too severe cognitive disorder to be assessed, patients with early stage of cognitive disorder without assessment and patients without any conclusive cognitive information.

We obtained informations about cognitive disorder from patients, proxy, family and general practitioners because the use of scales is not always appropriate to the acute phase of hospitalization [2]. We do think that our groups were well defined, considering the time of management of these patients in the acute and preoperative period before HF surgery, and differences between the 3 groups (especially DP/CSND vs NDP) have strengthened our inclusion criteria and group constitution:

- DP patients were less autonomous (ADL 3 [1-4]); they often lived in institutions (40%) and suffered more often from postoperative delirium (56%);

- NDP patients were more autonomous (ADL 6 [5-6]), they rarely lived in institutions (4%), and they suffered less often from postoperative delirium (26%).

4.3 Limits

This study had some limitations. It was an observational, single center study. Nonetheless, mono-centric studies ensure a high level of homogeneity in the way that data are collected and analyzed (we only had 11 patients lost to follow up). Although this study cannot conclude to a causal link, the impact of our orthogeriatric-dedicated unit on HF mortality in the population of patients with dementia should have been ideally studied by an interventional study (orthogeriatric-dedicated unit versus standard procedure). But, we previously published a study [26], showing that early admission to a dedicated geriatric unit improved 6-month mortality and morbidity in elderly patients with HF. After completion of this study [26], it could be considered not ethical to randomize patients between standard procedure and orthogeriatric-dedicated unit.

We did not have information about the degree of dementia and the date of diagnosis, known to be prognostic factors [11,12,15,23,37]. Because it was a retrospective study, we did not have systematic data on cognitive assessment at 6 months to better define CSND patients.

There is growing evidence from multiple studies that a similar benefit may be obtained elsewhere [2,39]. On these grounds, we anticipate that the deployment of new UPOG units in France as from 2014 will hopefully confirm these results, refine them and help find new ways to improve the outcome of patients facing HF surgery with or without cognitive disorders.

In conclusion, our study provides new information on the association between cognitive status before surgery and global outcomes. When cared for in a dedicated orthogeriatric care

pathway, the global prognosis (mortality and functional outcome) of patients with dementia seems to be the same as patients without dementia.

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Figure 1: Flow Chart


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┌─────────────────────────────────────────┐
│ Patients > 70 years old admitted with    │
│ hip fracture in UPOG (from 1st July 2009  │
│ to 31st December 2015)                    │
│              N = 711                      │
└─────────────────────────────────────────┘
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Excluded patients (some overlapped situations)

- Multiple fractures **(n = 36)**

- Metastatic fractures **(n= 8)**

-Fractures complicated by a previous hip prosthesis or osteosynthesis **(n= 44)**

Total: N = 61

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┌─────────────────────────────────────────┐
│           Selected patients               │
│             N = 650 (92%)                 │
└─────────────────────────────────────────┘
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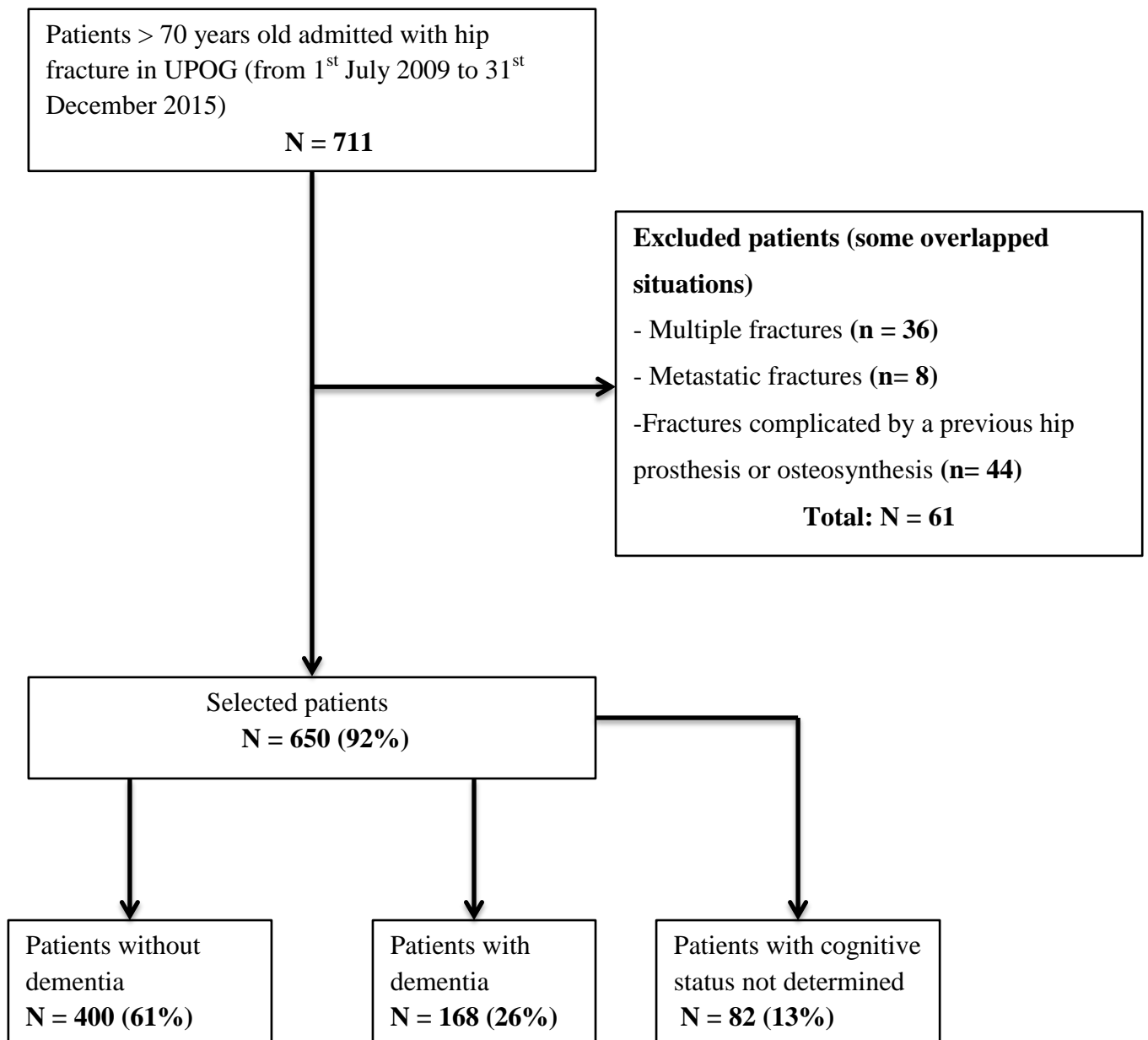| Patients without dementia **N = 400 (61%)** | Patients with dementia **N = 168 (26%)** | Patients with cognitive status not determined **N = 82 (13%)** |

Table 1: Characteristics of the population and comparison of the main characteristics in the 3 groups of patients: without dementia (NDP), with cognitive status not determined (CSND) and with dementia (DP)

	All patients N = 650	NDP N = 400	DP N = 168	CSND N = 82
Age (years)	86 ± 6	86 ± 6	87 ± 6 **	89 ± 6**$^{\$}$
Female	495 (76)	298 (74)	135 (80)	62 (76)
Medical history				
CIRS 52	9 [6 – 12]	8 [6 – 11]	10 [8 – 12]**	10 [8 – 13]**
Depression	56 (9)	23 (6)	25 (15)**	8 (10)
Stroke	112 (17)	66 (16)	34 (20)	12 (15)
Hypertension	453 (70)	282 (70)	114 (68)	57 (70)
Diabetes	78 (12)	54 (14)	12 (7)**	12 (15)
Obesity	42 (7)	32 (8)	6 (4)	4 (5)
Atrial fibrillation	177 (27)	101 (25)	47 (28)	29 (35)
Coronary artery disease	119 (18)	73 (18)	17 (29)	17 (21)
Cardiac failure	111 (17)	72 (18)	14 (23)	16 (20)
Thromboembolic disease	54 (8)	30 (10)	11 (7)	5 (6)
COPD	48 (8)	30 (8)	11 (7)	7 (9)
Chronic renal failure	341 (66)	252 (63)	118 (70)	61 (74)
Cancer	133 (20)	91 (23)	25 (15)**	17 (21)
Number of drugs per day	5 [3 – 8]	5 [3 – 8]	6 [4 – 8]**	5 [3 – 7] $^{\$}$
Autonomy				
ADL	5 [5 – 6]	6 [5 – 6]	3 [2 – 5]**	5 [3 – 6]** $^{\$}$
ADL = 6	340 (53%)	283 (71%)	33 (21%)	24 (30%)
Living in institution	102 (16)	16 (4)	73 (43)**	13 (16)** $^{\$}$
Living at home with assistance	517 (80)	292 (73)	157 (93)**	67 (82) $^{\$}$
Walking ability				
Walking	632 (97)	393 (98)	160 (95)**	79 (96)
Walking with assistance	332 (51)	184 (46)	101 (60)**	47 (57)
Repeated falls	316 (49)	151 (38)	119 (71)**	46 (56)** $^{\$}$
Fracture				
Intertrochanteric fracture	337 (52)	214 (56)	87 (52)	42 (51)
Femoral neck fracture	313 (48)	171 (44)	81 (48)	40 (49)
Surgery				
Time to surgery (h)	23 [14 – 36]	23 [14 – 33]	24 [14 – 37]	25 [13 – 42]
Time to surgery > 48 hours	89 (14)	40 (12)	24 (15)	16 (20)
Duration of surgery (min)	130 [110 – 160]	130 [110 – 160]	120 [110 – 150]	120 [100 – 147]**
Time to UPOG (h)	38 [25 – 63]	38 [26 – 66]	36 [25 – 64]	34 [24 – 57]
Gamma nail	339 (52)	207 (53)	84 (52)	38 (47)
Dynamic hip screw	54 (8)	31 (8)	8 (5)	10 (12)
Unipolar prosthesis	242 (38)	141 (36)	67 (41)	34 (42)
Bipolar prosthesis	15 (2)	12 (3)	3 (2)	0 (0)
Hemoglobin				
Preoperative hemoglobin (g.dL^{-1})	12.2 ± 1.6	12.3 ± 1.7	12.0 ± 1.7	12.1 ± 1.5
Preoperative anemia	294 (45)	171 (43)	83 (49)	40 (49)

- Data are mean ± SD, median [25–75 interquartile], or number (percentage).
- **: Comparison with NDP; $^{\$}$ Comparison with DP = p <0.05: Comparison between 3 groups was performed using the Kruskal Wallis test followed by the Dunn test for quantitative variables, and Fisher's exact method for qualitative variables
- CIRS: cumulative illness rating scale; COPD: chronic obstructive pulmonary disease; ADL: activity daily living; UPOG: post-operative geriatric unit. Obesity defined as body mass index > 30 kg.m2. Anemia was defined by Hb level < 12 g.dL^{-1} in women and 13 g.dL^{-1} in men. h = hours; m = minutes

Table 2. Post-operative complications and 6-month outcomes in the 3 groups of patients: without dementia (NDP), with cognitive status not determined (CSND) and with dementia (DP)

	All patients N = 650	NDP N = 400	DP N = 168	CSND N = 82
Time to first sitting (days)	1 [1 – 2]	1 [1 – 2]	1 [1 – 2]	1 [1 – 3] [$]
Time to first walking (days)	2 [1 – 4]	2 [1 – 4]	2 [1 – 3]	3 [2 – 4]** [$]
Post-operative complications				
Delirium	254 (39)	105 (26)	99 (59)**	50 (61)**
Pain	621 (96)	384 (96)	156 (93)	81 (99) [$]
Morphine administration	586 (90)	359 (90)	153 (91)	74 (90)
Min. in-hosp hemoglobin (g/dL^{-1})	9.2 ± 1.4	9.2 ± 1.4	9.3 ± 1.4	9.1 ± 1.6
In-hospital transfusion	357 (53)	223 (56)	87 (52)	47 (57)
Total packed RBC per patient	1 [0 – 2]	1 [0 – 2]	1 [0 – 2]	1 [0 – 2]
Stool impaction	277 (43)	164 (41)	78 (46)	35 (43)
Urinary retention	168 (26)	108 (27)	39 (23)	21 (26)
Pressure ulcer	79 (12)	47 (12)	20 (12)	12 (15)
Acute heart failure	83 (13)	54 (14)	13 (8)	16 (20) [$]
Acute coronary syndrome	68 (10)	40 (10)	17 (10)	11 (13)
Acute atrial fibrillation	57 (9)	34 (8)	16 (10)	7 (9)
Infection	121 (19)	68 (17)	37 (22)	16 (20)
Acute thromboembolism disease	29 (5)	16 (4)	7 (4)	6 (7)
Admission into ICU	31 (5)	23 (6)	3 (2)**	5 (6)
LOS (days)	11 [9 – 15]	11 [9 – 15]	11 [8 – 14]	13 [10 – 17]** [$]
Death during hospitalization	23 (4)	16 (4)	2 (1)	5 (6) [$]
Walking at discharge	568 (88)	351 (89)	149 (89)	68 (84)
Walking with assistance at discharge	546 (86)	344 (88)	138 (83)	64 (84)**
Admission to rehabilitation care	514 (79)	335 (84)	113 (67)**	66 (80) [$]
Home return[a]	102 (16)	41 (10)	51 (30)**	10 (12) [$]
After 6 months				
Walk with assistance (MD = 26)	331 (63)	209 (64)	85 (61)	37 (62)
ADL score (MD = 323)	4 [2 – 5]	5 [3 – 6]	2 [1 – 4]**	3 [2 – 5]** [$]
Newly institutionalized patients (MD = 11)	81 (12)	30 (8)	32 (19)**	10 (23)**
Death (MD = 11)	97 (15)	53 (14)	26 (16)	18 (22)**
Home return[a] (MD = 33)	464 (89)	296 (92)	118 (84)**	50 (85)

- Data are mean ± SD, median [25–75 interquartile], or number (percentage).
- **: Comparison with NDP; [$] Comparison with DP = p <0.05: Comparison between 3 groups was performed using the Kruskal Wallis test followed by the Dunn test for quantitative variables, and Fisher's exact method for qualitative variables
- ADL: activity daily living; UPOG: post-operative geriatric unit. LOS: length of stay. ICU: Intensive care unit. RBC: red blood cell
- MD: Missing data

Table 3. Multivariate logistic regression analysis predicting the risk of delirium, the opportunity to go to rehabilitation care at discharge, death and new institutionalization at 6 month

Variables	OR [95% CI]	P value
Prediction of delirium after surgery (AIC = 704)		
Age, reference value ≤ 80 years		
- Age 81-85	1.57 [0.85 – 2.96]	0.15
- Age 86-90	2.13 [1.21 – 3.83]	0.009*
- Age > 90	2.06 [1.12 – 3.85]	0.002*
Sex, reference value = female		
- Male = yes	1.52 [0.98 – 2.36]	0.06
CIRS 52, reference value ≤ 9		
- CIRS > 9	1.17 [0.78 – 1.76]	0.43
Number of drugs per day, reference value < 5		
- Number of drugs per day ≥ 5	0.99 [0.66 – 1.50]	0.99
Pre-fracture ADL6, reference value = 6		
- Pre-fracture ADL ≤ 5	1.67 [1.08 – 2.58]	0.02*
Walking before fracture without assistance, reference value = yes		
- Walking before fracture with assistance	0.81 [0.54 – 1.22]	0.32
Transfusion during hospitalization, reference value = No		
- Transfusion during hospitalization: Yes	1.74 [1.19– 2.55]	0.005*
Time to first sitting, reference value ≤ 1		
- Time to first sitting > 1	1.09 [0.75 – 1.59]	0.65
Time to surgery, reference value ≤ 48 hours		
- Delay > 48 hours	0.95 [0.56 – 1.61]	0.85
Cognitive status, reference value = Without dementia		
- Patients with dementia	3.12 [1.97 – 4.96]	< 0.001*
- Patients with cognitive status not determined	3.30 [1.87 – 5.80]	< 0.001*
Prediction of admission to rehabilitation care at discharge (AIC = 596)		
Age, reference value ≤ 80 years		
- Age 81-85	1.44 [0.72 – 2.95]	0.30
- Age 86-90	1.40 [0.74 – 2.76]	0.32
- Age > 90	1.45 [0.73 – 2.99]	0.29
Sex, reference value = female		
- Male = yes	0.99 [0.60 – 1.64]	0.98
CIRS 52, reference value ≤ 9		
- CIRS > 9	0.95 [0.60 – 1.51]	0.83
Number of drugs per day, reference value < 5		
- Number of drugs per day ≥ 5	1.05 [0.66 – 1.67]	0.82
Pre-fracture ADL6, reference value = 6		
- Pre-fracture ADL ≤ 5	2.36 [1.41 – 3.97]	0.001*
Walking before fracture without assistance, reference value = yes		
- Walking before fracture with assistance	0.60 [0.37 – 0.93]	0.02*
Time to surgery, reference value ≤ 48 hours		
- Delay > 48 hours	0.81 [0.43 – 1.45]	0.49
Delirium, reference value = no		
- Delirium = Yes	1.21 [0.77 – 1.88]	0.41
Cognitive status, reference value = Without dementia		
- Patients with dementia	1.53 [0.91 – 2.55]	0.10
- Patients with cognitive status not determined	0.90 [0.44 – 1.76]	0.77

Prediction of death at 6 month (AIC = 483)		
Age, reference value ≤ 80 years		
- Age 81-85	0.95 [0.41 – 2.19]	0.90
- Age 86-90	1.22 [0.58 – 2.66]	0.61
- Age > 90	1.38 [0.63 – 3.13]	0.43
Sex, reference value = female		
- Male = yes	1.55 [0.88 – 2.68]	0.12
CIRS 52, reference value ≤ 9		
- CIRS > 9	1.75 [1.04 – 2.98]	0.04*
Number of drugs per day, reference value < 5		
- Number of drugs per day ≥ 5	1.24 [0.72 – 2.18]	0.44
Pre-fracture ADL6, reference value = 6		
- Pre-fracture ADL ≤ 5	2.45 [1.40 – 4.38]	0.002*
Walking before fracture without assistance, reference value = yes		
- Walking before fracture with assistance	1.93 [1.13 – 3.39]	0.02*
Time to surgery, reference value ≤ 48 hours		
- Delay > 48 hours	1.21 [0.63 – 2.21]	0.55
Delirium, reference value = no		
- Delirium = Yes	1.01 [0.66 – 1.81]	0.70
Cognitive status, reference value = Without dementia		
- Patients with dementia	0.65 [0.35 – 1.17]	0.16
- Patients with cognitive status not determined	0.90 [0.44 – 1.80]	0.79

| **Prediction of new institutionalization at 6 month (AIC = 443)**		
Age, reference value ≤ 80 years		
- Age 81-85	1.03 [0.41 – 2.65]	0.95
- Age 86-90	1.27 [0.57 – 3.07]	0.57
- Age > 90	1.42 [0.61 – 3.54]	0.42
Sex, reference value = female		
- Male = yes	0.80 [0.40 – 1.51]	0.51
CIRS 52, reference value ≤ 9		
- CIRS > 9	1.08 [0.62 – 1.87]	0.78
Number of drugs per day, reference value < 5		
- Number of drugs per day ≥ 5	0.98 [0.56 – 1.75]	0.96
Pre-fracture ADL6, reference value = 6		
- Pre-fracture ADL ≤ 5	0.89 [0.49 – 1.65]	0.72
Walking before fracture without assistance, reference value = yes		
- Walking before fracture with assistance	2.00 [1.14 – 3.60]	0.02*
Time to surgery, reference value ≤ 48 hours		
- Delay > 48 hours	0.55 [0.22 – 1.20]	0.16
Delirium, reference value = no		
- Delirium = Yes	1.15 [0.67 – 1.97]	0.60
Cognitive status, reference value = Without dementia		
- Patients with dementia	2.56 [1.36 – 4.86]	0.003*
- Patients with cognitive status not determined	2.91 [1.37 – 6.07]	0.004*

CI: confidence interval; CIRS: cumulative illness rating scale; ADL: activity daily living; OR: Odds Ratio

AIC : Akaike Information Criterion

There was 11 missing data for death at 6 months and new institutionalization at 6 months; we excluded these patients from the analysis (1,7%).

Figure 2: Survival curves for mortality adjusted for age, sex, Cumulative Illness Rating Scale, number of drugs per day, pre-fracture ADL6, walking before fracture with assistance, time to surgery, delirium and cognitive status (calculated with a Cox regression analysis).
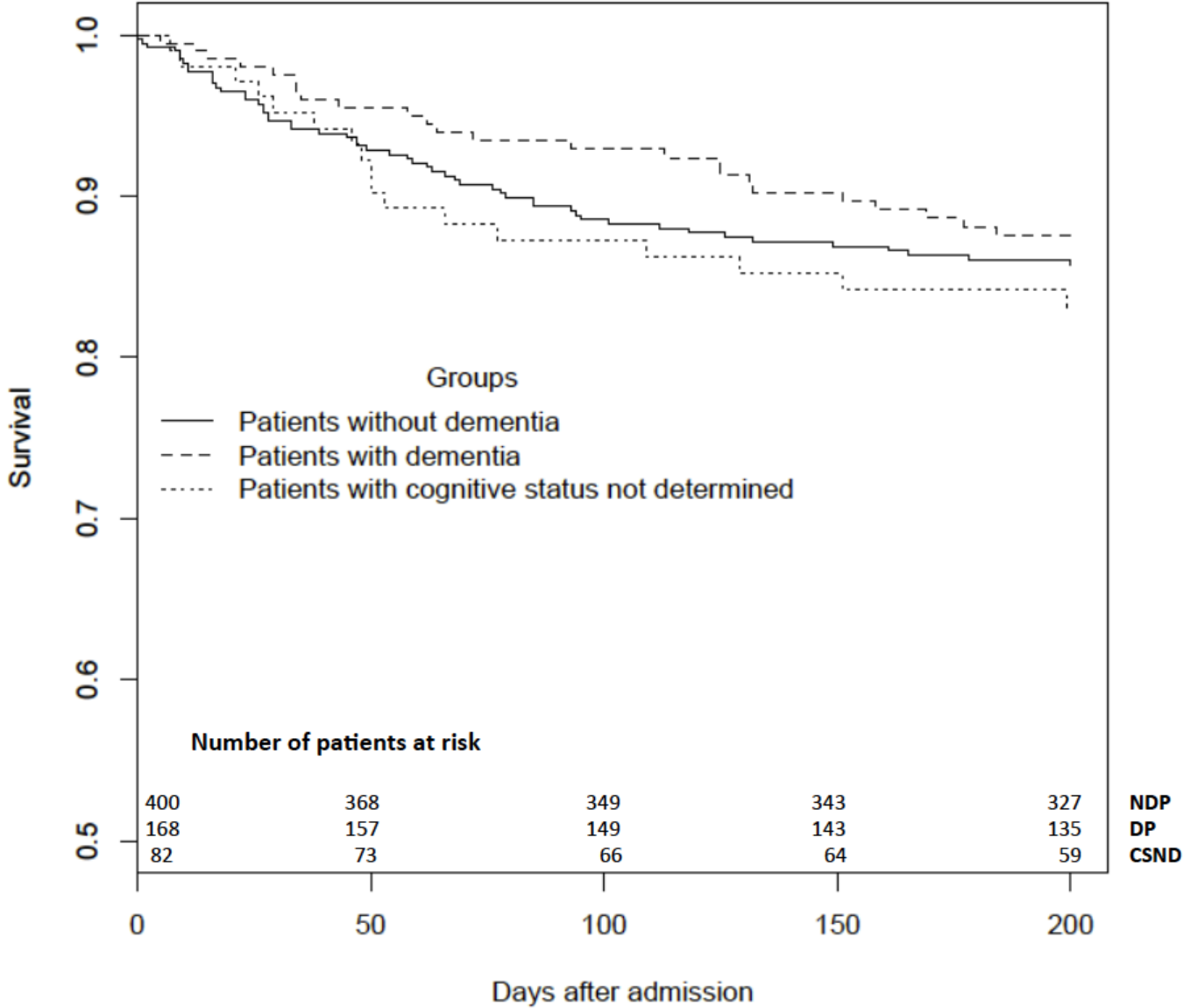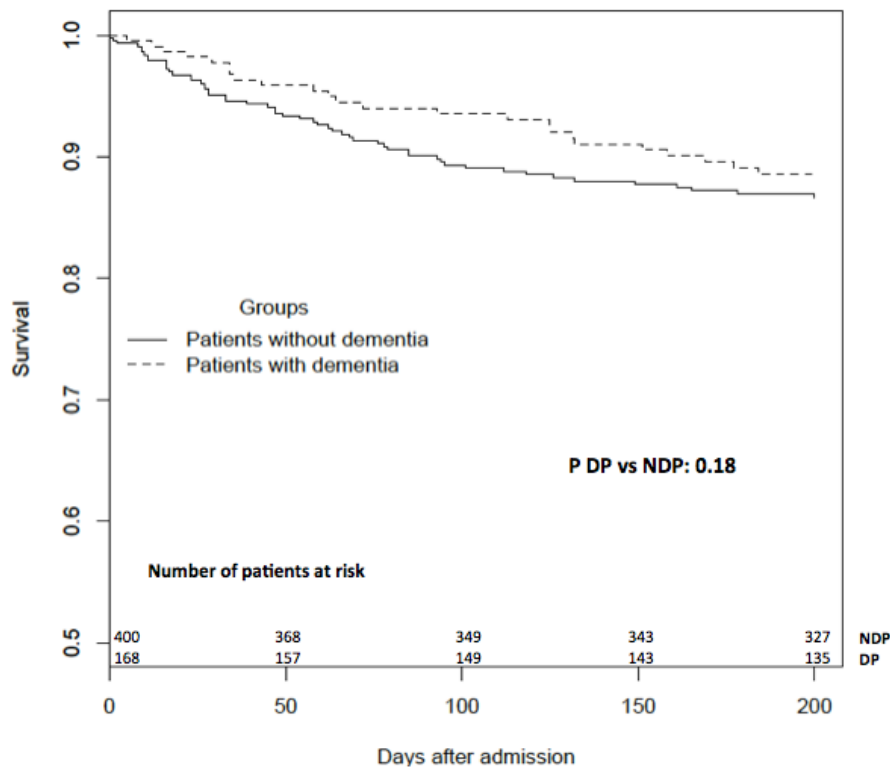

- P logrank: patients with dementia vs patient without dementia: 0.18; C Index = 0.60
- P logrank: patients with dementia vs cognitive status not determined: 0.29; C index = 0.70
- P logrank: cognitive status not determined vs patient without dementia: 0.62; C Index = 0.58

APPENDIX 1: Patients without dementia vs Patients with dementia: Multivariate cox proportional-hazards analysis predicting death and new-institutionalization in the first 6 months

Variables	Hazard Ratio [95% CI]	P value
Prediction of death		
Age, reference value ≤ 80 years		
- Age 81-85	0.91 [0.36 – 2.31]	0.85
- Age 86-90	0.63 [0.28 – 1.40]	0.25
- Age > 90	0.84 [0.36 – 1.98]	0.70
Sex, reference value = female		
- Male = yes	0.92 [0.50 – 1.70]	0.80
CIRS 52, reference value ≤ 9		
- CIRS > 9	1.24 [0.64 – 2.40]	0.52
Number of drugs per day, reference value < 5		
- Number of drugs per day ≥ 5	0.92 [0.50 – 1.72]	0.81
Pre-fracture ADL6, reference value = 6		
- Pre-fracture ADL ≤ 5	1.04 [0.53 – 2.02]	0.90
Walking before fracture without assistance, reference value = yes		
- Walking before fracture with assistance	1.67 [0.80 – 3.45]	0.17
Time to surgery, reference value ≤ 48 hours		
- Delay > 48 hours	1.54 [0.73 – 3.24]	0.26
Delirium, reference value = no		
- Delirium = Yes	1.21 [0.70 – 2.14]	0.48
Cognitive status, reference value = Without dementia		
- Patients with dementia	0.67 [0.38 – 1.20]	0.18

CI: confidence interval; CIRS: cumulative illness rating scale. *: P<0.05

[a]: Only patients who were not previously living in an institution were considered and death was considered as a censored observation.

Number of patients at risk

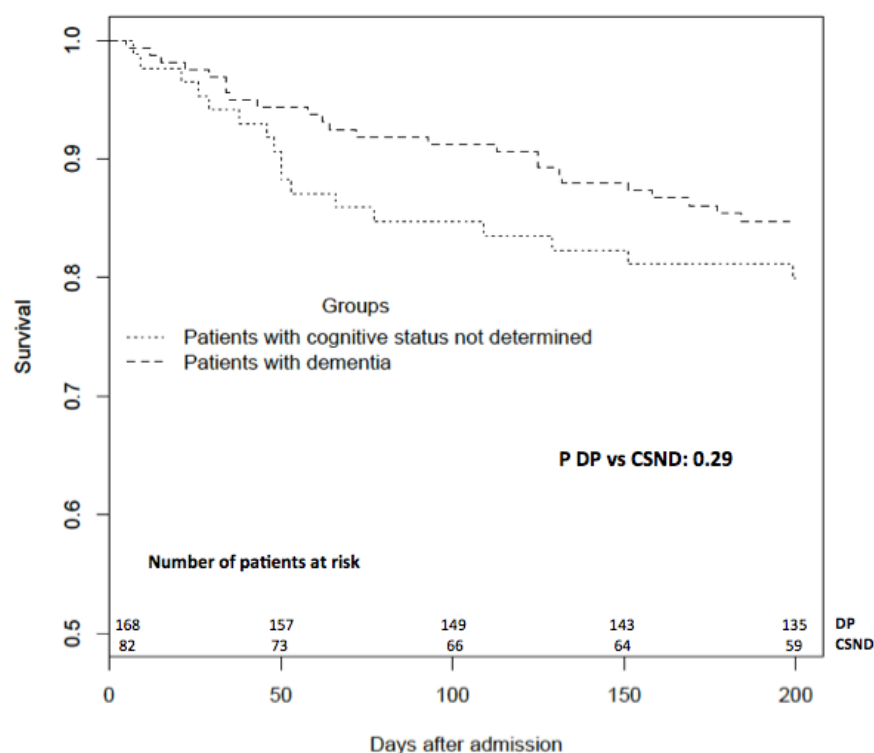|	0	50	100	150	200	
	400	368	349	343	327	NDP
	168	157	149	143	135	DP

P DP vs NDP: 0.18

APPENDIX 2: Patients with dementia vs Patients with cognitive status non determined: Multivariate cox proportional-hazards analysis predicting death and new-institutionalization in the first 6 months

Variables	Hazard Ratio [95% CI]	P value
Prediction of death		
Age, reference value ≤ 80 years		
- Age 81-85	0.64 [0.14 – 2.97]	0.57
- Age 86-90	1.35 [0.35 – 5.21]	0.66
- Age > 90	0.64 [0.16 – 2.60]	0.53
Sex, reference value = female		
- Male = yes	0.65 [0.22 – 1.96]	0.44
CIRS 52, reference value ≤ 9		
- CIRS > 9	0.71 [0.30 – 1.70]	0.45
Number of drugs per day, reference value < 5		
- Number of drugs per day ≥ 5	0.80 [0.29 – 2.26]	0.68
Pre-fracture ADL6, reference value = 6		
- Pre-fracture ADL ≤ 5	0.16 [0.04 – 0.65]	0.009*
Walking before fracture without assistance, reference value = yes		
- Walking before fracture with assistance	0.62 [0.24 – 1.61]	0.32
Time to surgery, reference value ≤ 48 hours		
- Delay > 48 hours	1.40 [0.52 – 3.77]	0.51
Delirium, reference value = no		
- Delirium = Yes	1.90 [0.72 – 5.03]	0.19
Cognitive status, reference value = cognitive status not determined		
- Patients with dementia	0.65 [0.28 – 1.45]	0.29

CI: confidence interval; CIRS: cumulative illness rating scale. *: P<0.05

[a]: Only patients who were not previously living in an institution were considered and death was considered as a censored observation.

APPENDIX 3: Patients without dementia vs patients with cognitive status non determined: Multivariate cox proportional-hazards analysis predicting death and new-institutionalization in the first 6 months

Variables	Hazard Ratio [95% CI]	P value
Prediction of death		
Age, reference value ≤ 80 years		
- Age 81-85	0.95 [0.38 – 2.34]	0.91
- Age 86-90	0.60 [0.25 – 1.45]	0.26
- Age > 90	0.64 [0.27 – 1.51]	0.31
Sex, reference value = female		
- Male = yes	0.78 [0.43 – 1.44]	0.43
CIRS 52, reference value ≤ 9		
- CIRS > 9	0.99 [0.53 – 1.86]	0.99
Number of drugs per day, reference value < 5		
- Number of drugs per day ≥ 5	1.02 [0.55 – 1.91]	0.94
Pre-fracture ADL6, reference value = 6		
- Pre-fracture ADL ≤ 5	1.11 [0.58 – 2.15]	0.74
Walking before fracture without assistance, reference value = yes		
- Walking before fracture with assistance	1.70 [0.86 – 3.38]	0.13
Time to surgery, reference value ≤ 48 hours		
- Delay > 48 hours	1.32 [0.67 – 2.61]	0.42
Delirium, reference value = no		
- Delirium = Yes	1.25 [0.71 – 2.21]	0.43
Cognitive status, reference value = Without dementia		
- Patients with cognitive status not determined	0.84 [0.41 – 1.68]	0.62

CI: confidence interval; CIRS: cumulative illness rating scale. *: P<0.05

[a] Only patients who were not previously living in an institution were considered and death was considered as a censored observation.