End of life management in Internal Medicine Wards: a single-center real-life report

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ABSTRACT

The burden of end of life in Internal Medicine wards is not negligible. However, literature evidence about the end-of-life care in Internal Medicine wards lacks. Therefore, this study aimed to report on end-of-life management in an Internal Medicine ward. We performed a retrospective study focusing on the characteristics and management of patients who consecutively died in an Italian Internal Medicine ward between July 1, 2018 and June 30, 2019. Demographic, co-morbidity, pharmacological treatment at hospital admission, and in the last 48-hours of life and procedures during hospital stay were collected. The study population was composed of 354 patients (190 females), corresponding to about ten percent of patients admitted to the ward, with a mean age ± standard deviation 83.5±10.6 years. Eighty-four percent of deaths was expected in the last 48 h before exitus. The main co-morbidities were blood hypertension (66.3%), solid or hematological malignancies (40.3%), arrhythmias (34.7%), pressure ulcers (31.3%), and diabetes (27.4%). The main causes of hospitalization were infectious diseases (23.1%) and cardiac or respiratory failure (20.9%). In seven percent of patients, palliative care had already been activated before the hospital admission. No patient had written living wills or advance directives. In the last 48 hours of life, the main pharmacological classes prescribed were opioids (63.2%), antibiotics (46.9%), and corticosteroids (46.3%). Compared with pharmacological classes prescribed at hospital admission, in the last 48 h of life, the prescription of antibiotics, corticosteroids, opioids, and benzodiazepines increased significantly, whereas the prescription of antihypertensive agents, proton pump inhibitors, and antithrombotic drugs resulted notably reduced. A written order to withdraw vital parameters acquisition or active treatment were found in 30.7% and 31.9%, respectively. In the last 48 h of life, 61% of patients underwent at least one blood assay, 34% arterial blood gas analysis, and about 35% at least one among radiography, computer tomography, magnetic resonance, or endoscopy. During the hospital stay, 9% of patients underwent blood transfusion. 28.1% of patients received a blood transfusion in the last 48 hours of life. Appropriate management of end of life represents a challenge in Internal Medicine wards.

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Introduction

The burden of *end of life* in Internal Medicine wards is absolutely not negligible. In Italy, Internal Medicine wards encompass the majority of hospital admissions. Patients admitted to Internal Medicine wards are typically old or very old, fragile, complex, and complicated.[1] Many of these patients suffer from chronic and/or degenerative diseases, which cause severe co-morbidities, influencing the prognosis of acute diseases for whom the patients are admitted to the hospital.[1] In many Italian Hospitals, beds reserved to specialties such as Oncology, Hematology, Neurology, *etc*. lack, therefore, patients suffering from advanced diseases such as solid or hema-

tological cancers or severe neurological disorders are admitted to Internal Medicine wards and managed by the support of specialty consultants. The INDOMITO Study, performed in Internal Medicine wards of Tuscany, Italy, showed that Internal Medicine admissions account for 21% of all acute hospital admissions and one-half of non-surgical admissions.[2] In Tuscany, Italy, in-hospital mortality in Internal Medicine wards ranges from 6% to 10%. Moreover, many patients discharged to home health care or nursing homes are at the end of life and/or need palliative care.

Despite this burden, literature evidence about the end-of-life care in Internal Medicine wards lacks. Therefore, the aim of this study was to report on the end-of-life management in an Internal Medicine ward.

Materials and Methods

We retrospectively collected demographic, clinical, and assistance data and diagnostic-therapeutic work-up of patients who consecutively died in one year (July 1, 2018-June 30, 2019) in the Internal Medicine II ward of Empoli, Italy. We analyzed age, sex, marital status, presence of written living wills or advance directives, causes of hospitalization, length of hospital stay (LOS), co-morbidity, activation of palliative care before hospitalization, Modified Early Warning Score (MEWS) at ward admission, pharmacological treatment prescribed at ward admission and in the last 48 h of life, procedures performed during hospitalization such as radiographies, computer tomographies (CT), magnetic resonances (MR), endoscopies, biopsies, blood transfusions, chemotherapy or radiotherapy, blood assays, arterial blood gas analyses, *etc*. Moreover, we collected data about artificial nutrition, central venous accesses, and urinary catheterism. The Local Ethical Committee approved the study (authorization number 16132_oss, protocol code: CDO – 019).

Statistical analysis

Continuous variables were reported as mean ± standard deviation (SD) when normally distributed, as median and interquartile range (IQR) when not normally distributed. Categorical variables were analyzed by using the Fisher exact test, as appropriate. A P-value <0.05 was considered significant.

Results

In the analyzed period, 3,588 patients were admitted to the Internal Medicine II of Empoli, Italy. Of them, 354 (9.8%), 164 males and 190 females, with mean age±SD 83.5±10.6 years (range 22-99) died during hospitalization. 83.6% of patients was 75-years old and older, and 51.3% was widow or widower. Median LOS was 4 days (IQR 2-8), mean LOS±SD was 6.3±7.3 days. In about 85%, death was expected or probable in the last 48 hours before exitus. Table 1 summarizes the general characteristics of patients.

The main co-morbidities were blood hypertension (66.3%), solid or hematological malignancies (40.3%), arrhythmias (34.7%), pressure ulcers (31.3%), and diabetes. Seven percent of patients had activated palliative cares before hospitalization. No patient had living wills or advance directives. Table 2 shows co-morbidities.

The main causes of hospitalization were infectious diseases (23.1%), cardiac or respiratory failure (20.9%), and acute stroke (13.8%) (Table 3).

Median MEWS (IQR) at ward admission was 2 (IQR 1-3), and the median (IQR) time of MEWS acquisition was 4 (IQR 1-7). A written order for MEWS or active treatment withdrawal was found in 30.7% and 31.9% of patients, respectively.

Antihypertensive agents (59.3%), antiplatelets or anticoagulants (55.9%), proton pump inhibitors (54.5%), diuretics (41.2%), corticosteroids (27.6%), antidiabetics (27.4%), and antibiotics (25.9%) were

Table 1. General characteristics of patients.

Number	354
Males/Females	164/190
Marital status (based on available data of 298 patients)	
Unmarried	10 (3.3%)
Married	134 (45%)
Widower/Widow	153 (51.3%)
Divorced	1 (0.4%)
Mean age ± SD, yrs	83.5±10.6
Median age (IQR), yrs	86 (80-90)
Mean lenght of hospital stay ± SD, days	6.3±7.3
Median lenght of hospital stay (IQR), days	4 (2-8)
Expected death in the last 48 h	300 (84.7%)
Written living wills and/or advance directive	0 (0%)

SD, standard deviation; yrs, years; IQR, interquartile range.

the most prescribed pharmacological classes at ward admission, whereas opioids (63.2%), antibiotics (46.9%) and corticosteroids were given in the last 48 h of life. Figure 1 shows the difference between drugs prescribed at ward admission and in the last 48 h of life. Comparing them it is possible to state that antibiotics, corticosteroids, opioids, and benzodiazepines were significantly more prescribed in the last 48 h, whereas the prescription of antihypertensive and antithrombotics was significantly lower. Table 4 shows the distribution of palliative drugs prescribed in the last 48 h of life. In more than sixty percent of patients, morphine was prescribed, while in one-fourth of patients it was midazolam.

Sixty-one percent of patients and thirty-four percent of patients underwent at least one blood assay and arterial blood gas analysis in the last 48 h of life. About one-third of patients received artificial nutrition during hospitalization, 22.8% by nasogastric tube (NGT), 3.1% by percutaneous endoscopic gastrostomy (PEG), 8.7% by parenteral line. About seventy-two percent of patients had urinary catheterism, while about fourteen percent had a central venous catheter (CVC) or peripherally inserted central catheter (PICC). In 38.7% of patients, NGT, PEG, CVC, or PICC were inserted during hospitalization, while in 11%, one of these devices was present before hospitalization (Table 5).

From Emergency Department arrival to death, more than one-half of patients underwent at least one radiography, 33.6% one CT or MR, 9% one red cell or platelet transfusion (Table 6). Of patients who underwent transfusion, 28.1% received a transfusion in the last 48 h of life. In the last 48 h of life, 31.9% of patients underwent at least one radiography, CT, MR, or endoscopy.

Table 2. Co-morbidity.

	N (%)
Blood hypertension	235 (66.3%)
Solid or haematologic cancer	143 (40.3%)
Arrythmias	123 (34.7%)
Pressure ulcers	111 (31.36%)
Diabetes	97 (27.40%)
Dementia	87 (24.58%)
Ischemic heart diseases	84 (23.73%)
Respiratory failure	82 (23.16%)
Chronic obstructive pulmonary disease	80 (22.60%)
Previous ischemic or hemorrhagic stroke	76 (21.47%)
Heart failure	73 (20.62%)
Immobilization	6 (18.64%)
Other neurological disease	53 (14.97%)
Renal failure	51 (14.41%)
Reumatic disease	35 (9.89%)
Peripheral artery disease	33 (9.32%)
Parkinson disease	15 (4.24%)
HIV/HBV/HCV positivity	4 (1.13%)

Discussion

To date, the management of the end of life and appropriate use of palliative care in Internal Medicine wards are neglected topics. The reason of it could be ascribed to the lack of training courses about the end of life and palliative cares addressed to physicians and nurses working in Internal Medicine wards. In fact, traditionally, the clinical and nursing competence of the staff of the Internal Medicine wards has been mainly oriented to the care of acute diseases and poorly oriented to the complexity of care of patients near to death. Consequently, most diagnostic procedures and therapeutical interventions, together with hospital admissions, fall in the last three months of life. Despite this approach in the last months of life, quality of life and life expectation seem not improved, whereas costs of healthcare systems increase steadily. A study performed in three Australian hospitals showed that the incidence of futile treatments during the end of life was 12.1% encompassing 153.1 million of Australian dollars per year.[3] In Tuscany, Italy, in the last three months of life, a surge in costs for hospital admissions in patients suffering from chronic diseases or cancer occurs.[4] This study shows that 55% of patients suffering from cancer and 65% of patients with chronic diseases who die have at least one access to the Emergency Department in the last month before death and 73% of patients with cancer

Table 3. Main causes of hospital admission.

	N (%)
Infectious diseases*	2 (23.1%)
Cardiac or respiratory failure	74 (20.9%)
Acute stroke	49 (13.8%)
Acute gastrointestinal diseases	16 (4.5%)
Miscellaneous	133 (37.5%)

*Pneumonia, urinary tract infections and/or other infections

Table 4. Palliative pharmacological treatment in the last 48 h of life.

Morphine	219 (61.8%)
Midazolam	4 (26.5%)
Hyoscine-N-butylbromide	96 (27.1%)
Haloperidol	27 (7.6%)

and 76% of patients with chronic diseases receive at least one hospital admission in the last month before death.[4] The Hospital, particularly the Internal Medicine wards, seem to represent the primary resource for managing end-of-life patients, despite alternative options such as palliative home care and Hospices are nowa-

Table 5. Artificial nutrition, central venous accesses, and urinary catheterism.

Artificial enteral nutrition	
Nasogastric tube (NGT)	81 (22.8%)
Percutaneous endoscopy gastrostomy (PEG)	11 (3.1%)
Artificial parenteral nutrition (APN)	31 (8.7%)
Central venous catheterism (CVC)/peripheral inserted central catheterism (PICC)	50 (14.1%)
Urinary catheter	253 (71.4%)
NGT/PEG/APN/CVC-PICC inserted during hospitalization	137 (38.7%)
NNG/PEG/APN/CVC-PICC present before hospitalization	39 (11.0%)

Table 6. Procedures performed during hospitalization.

Chemotherapy	5 (1.4%)
Radiotherapy	3 (0.8%)
Red cells or platelets transfusion	32 (9%)
Dyalisis	0 (0%)
Radiography	192 (54%)
Computer tomography	119 (33.6%)
Magnetic resonance	6 (1.6%)
Endoscopy	12 (3.4%)
Biopsy	5 (1.4%)
Red cells or platelets transfusion performed in the last 48 h of life	9 (2.54%)
Radiography, computer tomography, magnetic resonance and/or endoscopy performed in the last 48 h of life	13 (31.92%)

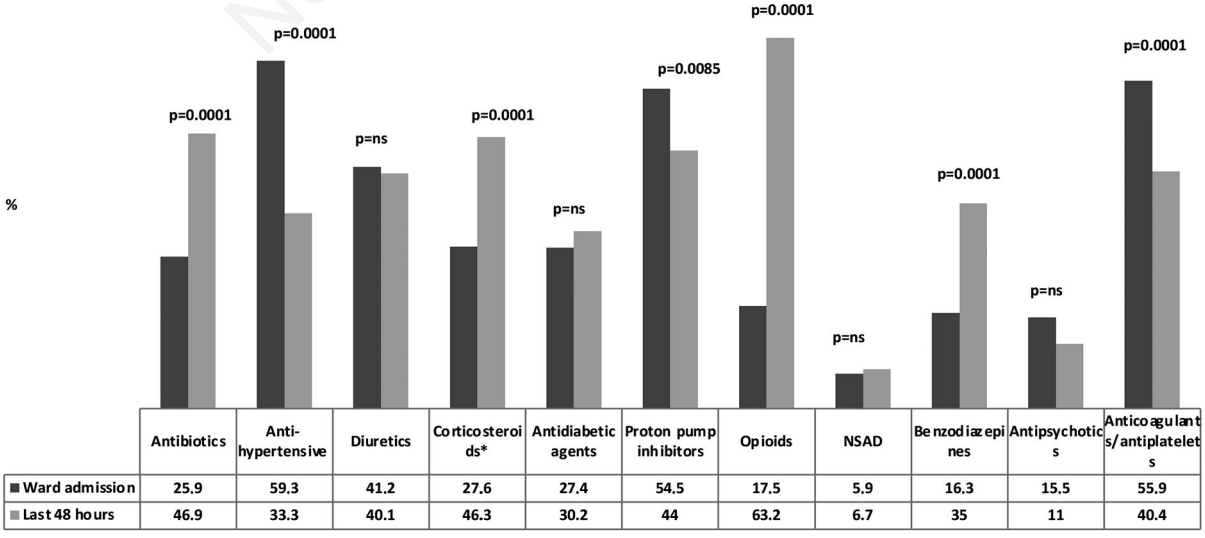

Figure 1. Pharmacological treatment at ward admission and in the last 48 h of life.

days widespread. However, many patients are admitted to Hospices too late. In Tuscany, Italy, between patients who are admitted to Hospice, 60% of them are admitted in the last week of life.[4] All this in the face of a lack of attention of symptoms such as dyspnea, pain, distress, death rattle, agitation, nausea and/or vomiting, which should be treated by using competence in palliative care. A Canadian study performed in 480 patients (28% of them admitted to Internal Medicine wards) suffering from similar co-morbidity to the one found in our study showed that in the last 48 h of life one-half of patients suffers from at least one symptom among dyspnea, pain, agitation, or nausea and thirty percent of them has two of these symptoms.[5] A study performed in Spain on about 1500 patients with median age 84 years who died in Internal Medicine wards found as main symptoms and clinical conditions dyspnea, anorexia, immobilization syndrome, and pain.[6] In this study, about 75% of patients had two or more diseases, and 52% were defined terminal. The Authors found a significant difference in awareness of being at the end of life between cancer and non-cancer patients (54.4% *vs* 15.5%, P<0.001).[6]

Thus, the appropriate management of the end of life represents a challenge for the modern Internal Medicine. Starting with the awareness of cultural and training gaps, Internal Medicine Societies should face up to the end of life topic with strong and concrete measures. A decalogue for the appropriate management of the end of life has been drawn up and distributed by the Italian Scientific Society of Hospital Internal Medicine FADOI. This decalogue suggests refraining from invasive procedures and/or interventions in Internal Medicine patients at the end of life, selecting care aimed to improve the quality of life and effective treatment of pain.[7,8] In this context, of much interest are the five Choosing Wisely indications from the American Academy of Hospice and Palliative Medicine. Between them: i) NGT and/or PEG should be avoided in patients with severe cognitive impairment; ii) palliative care should be activated as soon as possible in patients with unfavorable prognosis; iii) withdrawal of palliative radiotherapy in patients with metastatic bone cancer.[9]

Despite the above-mentioned considerations, literature evidence about the end of life and palliative care in Internal Medicine lacks, and the poor evidence is difficult to extrapolate and reproduce in clinical practice because not homogeneous, often retrospective and not designed in randomized clinical trials. To focus on the management of clinical, therapeutical, assistance, and palliative aspects of patients at the end of life in Internal Medicine, our study could give many answers about the characteristics of patients who die in this context. The resulting picture demonstrates that patients who die in Internal Medicine wards are very old and poly-pathological, have a low median LOS before death, and in about 85% of them, the death is expected in the last 48 h of life. Despite this, a not negligible percentage of patients undergoes multiple pharmacological treatments, diagnostic procedures often invasive, artificial nutrition, blood transfusion, and receives monitoring of vital parameters and nursing assistance such as acute patients. Although in many patients, this approach could be justified due to hospital admission for acute diseases or exacerbation of chronic diseases, the performance of pharmacological treatment and/or diagnostic procedures in patients with advanced chronic-degenerative diseases or unfavorable prognosis such as advanced cancer, could be futile and unappropriate. Written living wills or advance directives could address to a more appropriate management of the end of life. However, the awareness to write living wills and/or advance directives is uncommon, especially in the elderly. In our study, no patients had written living wills and/or advance directives, despite in Italy, advance directives are regulated by law since the end of 2017.

A multidisciplinary approach by physicians and nurses and effective communication to patients, relatives and/or caregivers are fundamental for the appropriate management of the end of life. The sharing between the staff of Internal Medicine wards about the appropriate management of patients at the end of life starts from the appropriate identification of patients, such as suggested from NICE guidelines,[10] followed by dignity-oriented treatments aimed to improve quality of life and reduce the suffering. Thus, the widespread use of screening tools aimed to identify patients at the end of life, such as the NecPAL score and the Palliative Prognostic Index[11,12] is fundamental.

In our study, we found that the most used drugs in the last hours of life are not only opioids, benzodiazepines, and corticosteroids, which have demonstrated to reduce the suffering,[13,14] but also antibiotics, proton pump inhibitors, and antithrombotics. Of note, we found that in the last 48 h of life, compared with hospital admission, antibiotics prescription increases from 25% to 50%, whereas proton pump inhibitors and antithrombotics are yet prescribed in the last 48 h of life in about 40% of patients. The excessive use of antibiotics in the last phase of life is a widespread practice and it is a hot and debated topic in literature.[15] Previous studies demonstrated that about 90% of advanced cancer patients receive at least an antibiotic in the last week of life, and about 45% of nursing home residents suffering from severe cognitive impairment receive antibiotics in the last fifteen days before death.[16,17] Recently, an Australian study showed that about 70% of patients who die in the Hospital receive antibiotics and one-third of them continue to receive antibiotics despite physicians consider them futile in that context. Ninety-six percent of patients receive intravenous administration of antibiotics, and the most

prescribed antibiotic is piperacillin/tazobactam.[18]

Finally, our study demonstrates that there is an unmet need for education and training courses on appropriate management of the end of life. Skills on this topic are fundamental. Evidence shows that educational training could improve the management of symptoms and discomfort of end-of-life patients. Of much interest, in more than five thousand Internal Medicine patients some years ago, the FADOI-DOMINO Study showed that 37.5% of them suffered from pain and that after the educational program, the use of appropriate treatment to reduce pain was increased in about 73% of patients.[18]

We recognize that our study has limitations due to retrospective design, small sample size, and single-center location. Moreover, the end-of-life management could be influenced by subjectivity, skills, and personal experience of physicians and nurses of wards where patients spend their last hours. Furthermore, a lot of diagnostic-therapeutic-assistance decisions could be influenced by specialty consultants. Many results could be influenced by the lack of standardized protocols and the disagreement choices of patients, relatives, or caregivers. Despite these limitations, our study could be a starting point for future research on the end of life in Internal Medicine wards.

Conclusions

Management of patients at the end of life in Internal Medicine wards is frequent in clinical practice. Lack in training, standardized protocols, and the difficulty to make decisions on end-of-life patients due to multiple factors such as clinical, cultural, religious, social, psychological, *etc*. could prove an inappropriate management of the end of life and to bring to inadequate attention to the quality of life and suffering reduction. A call to action for appropriate management of the end of life in Internal medicine wards is warranted. Based on our experience, the Azienda USL Toscana Centro has started an educational program aimed to improve skills in the management of the end of life. A physician and a nurse from each of the thirteen Internal Medicine wards of this company will participate each year in an educational program consisting of one week of lectures and stage on the job in a Hospice. In 2019, an educational program was completed.

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