

Pattern of Comorbidities among Colorectal Cancer Patients in Spain

Miguel Angel Luque-Fernandez, Daniel Redondo-Sánchez,
Miguel Rodriguez-Barranco, M Carmen Carmona-Garcia,
Rafael Marcos-Gragera, Maria Jose Sanchez

Granada Cancer Registry, Andalusian School of Public Health
Biomedical Research Institute of Granada, University of Granada
CIBER of Epidemiology and Public Health
Catalan Institute of Oncology

University Hospital Dr Josep Trueta of Girona

Descriptive Epidemiology, Genetics and Cancer Prevention of the Biomedical Research Institute of Girona, University of Girona

<https://maluque.netlify.com/>

Colorectal Cancer

- Colorectal cancer (CRC) was the most frequently diagnosed cancer (i.e., adding the total number of cases of both sexes as a whole) in **Spain**, in 2015.[1]

Colorectal Cancer

- Colorectal cancer (CRC) was the most frequently diagnosed cancer (i.e., adding the total number of cases of both sexes as a whole) in **Spain**, in 2015.[1]
- Approximately 60% of CRC patients are older than 70 years. CRC incidence is likely to increase in the near future ([Grey Tsunami](#)).[2]

Colorectal Cancer

- Colorectal cancer (CRC) was the most frequently diagnosed cancer in both sexes as a whole in **Spain**, in 2015.[1]
- Approximately 60% of colorectal cancer patients are older than 70 years. CRC incidence is likely to increase in the near future ([Grey Tsunami](#)).[2]
- **Ageing**, increased life expectancy and life style changes may contribute to this increase.

Colorectal Cancer

- Colorectal cancer (CRC) was the most frequently diagnosed cancer in both sexes as a whole in **Spain**, in 2015.[1]
- Approximately 60% of colorectal cancer patients are older than 70 years. CRC incidence is likely to increase in the near future ([Grey Tsunami](#)).[2]
- **Ageing**, increased life expectancy and life style changes may contribute to this increase.
- Furthermore, the presence of **comorbidities** or **multi-morbidity** is highly prevalent among older cancer patients (≥ 70 years).[3]

Colorectal Cancer

- Colorectal cancer (CRC) was the most frequently diagnosed cancer in both sexes as a whole in **Spain**, in 2015.[1]
- Approximately 60% of colorectal cancer patients are older than 70 years. CRC incidence is likely to increase in the near future ([Grey Tsunami](#)).[2]
- **Ageing**, increased life expectancy and life style changes may contribute to this increase.
- Furthermore, the presence of **comorbidities** or **multi-morbidity** is highly prevalent among older cancer patients (≥ 70 years).[3]

[1] Galceran, J., et al., Cancer incidence in Spain, 2015. Clin Transl Oncol, 2017;19: 99-825

[2] Millan, Monica et al. Treatment of Colorectal Cancer in the Elderly. World Journal of Gastrointestinal Oncology. 2015: 204-220

[3] van Leersum NJ, et al. Increasing prevalence of comorbidity in patients with colorectal cancer in the South of the Netherlands 1995-2010. Int J Cancer.2013; 132(9): 2157-63

Comorbidity and multi-morbidity definitions

- **Comorbidity** is the existence of a long-term health condition or disorder in the presence of a primary disease of interest, such as cancer.[4]

Comorbidity and multi-morbidity definitions

- **Comorbidity** is the existence of a long-term health condition or disorder in the presence of a primary disease of interest, such as cancer.[4]
- **Multi-morbidity** refers to the existence of **two or more** long-term health conditions where at least 1 of these conditions must be a physical health condition.[5, 6]

Comorbidity and multi-morbidity definitions

- **Comorbidity** is the existence of a long-term health condition or disorder in the presence of a primary disease of interest, such as cancer.[4]
- **Multi-morbidity** refers to the existence of **two or more** long-term health conditions where at least 1 of these conditions must be a physical health condition.[5, 6]
- **Comorbidity** and **multi-morbidity** can **influence treatment options** in CRC patients.[7]

Comorbidity and multi-morbidity definitions

- **Comorbidity** is the existence of a long-term health condition or disorder in the presence of a primary disease of interest, such as cancer.[4]
- **Multi-morbidity** refers to the existence of **two or more** long-term health conditions where at least 1 of these conditions must be a physical health condition.[5, 6]
- **Comorbidity** and **multi-morbidity** can **influence treatment options** in CRC patients.[7]

[4] Porta, M.S., et al., A dictionary of epidemiology. Sixth edition. 2014, Oxford: Oxford University Press. xxxii, 343 pages.

[5] Lujic, S., et al., Multi-morbidity in Australia: Comparing estimates derived using administrative data sources and survey data. PLoS One, 2017. 12(8): p. e0183817.

[6] Multimorbidity: clinical assessment and management NICE guideline. September 2016. <https://www.nice.org.uk/guidance/ng56>

[7] Sarfati, D., B. Koczwara, and C. Jackson, The impact of comorbidity on cancer and its treatment. CA Cancer J Clin, 2016. 66(4): p. 337-50.

Pattern of Comorbidities among CRC Patients

There is consistent evidence showing the influence of **comorbidities** and **multi-morbidity** on **cancer outcomes** among CRC patients, but little evidence is available regarding the **descriptive pattern** of comorbidities/multi-morbidity and **risk factors** associated to their presence.

To study the Pattern of Comorbidities among CRC Patients

Thus, we described the **frequency** and **distribution** of comorbidities and multimorbidity as well as the risks factors associated with their presence among a cohort of CRC patients.

Methods: Study design

- We developed a **population-based cohort study** including all CRC incident cases (C18-C21), according to the International Classification of Diseases for Oncology, 3rd Edition, (ICD-O-3) diagnosed in the year 2011 and follow-up until December 31st, 2016, from two Spanish cancer registries: **Girona and Granada**, with **1,061** cases.



Data source

- Data from Spanish cancer registration was complemented with information from patient's **clinical medical records**.

Data source

- Data from Spanish cancer registration was complemented with information from patient's **clinical medical records**.
- Data were drawn following a detailed protocol from the European high-resolution studies collaboration **HIGHCARE project - Eranet TRANSCAN**: <http://www.hrstudies.eu/highcare.html>.

Data source

- Data from Spanish cancer registration was complemented with information from patient's **clinical medical records**.
- Data were drawn following a detailed protocol from the European high-resolution studies collaboration **HIGHCARE project - Eranet TRANSCAN**: <http://www.hrstudies.eu/highcare.html>.
- Information regarding cancer stage at diagnosis (TNM, 7th Ed.), cancer diagnostic exams, tumor morphology, cancer treatment, patients' comorbidities, performance and vital status was classified in three main categories of analysis:

Data source

- Data from Spanish cancer registration was complemented with information from patient's **clinical medical records**.
- Data were drawn following a detailed protocol from the European high-resolution studies collaboration **HIGHCARE project - Eranet TRANSCAN**: <http://www.hrstudies.eu/highcare.html>.
- Information regarding cancer stage at diagnosis (TNM, 7th Ed.), cancer diagnostic exams, tumor morphology, cancer treatment, patients' comorbidities, performance and vital status was classified in three main categories of analysis:
 - Patient characteristics

Data source

- Data from Spanish cancer registration was complemented with information from patient's **clinical medical records**.
- Data were drawn following a detailed protocol from the European high-resolution studies collaboration **HIGHCARE project - Eranet TRANSCAN**: <http://www.hrstudies.eu/highcare.html>.
- Information regarding cancer stage at diagnosis (TNM, 7th Ed.), cancer diagnostic exams, tumor morphology, cancer treatment, patients' comorbidities, performance and vital status was classified in three main categories of analysis:
 - Patient characteristics
 - Tumor factors

Data source

- Data from Spanish cancer registration was complemented with information from patient's **clinical medical records**.
- Data were drawn following a detailed protocol from the European high-resolution studies collaboration **HIGHCARE project - Eranet TRANSCAN**: <http://www.hrstudies.eu/highcare.html>.
- Information regarding cancer stage at diagnosis (TNM, 7th Ed.), cancer diagnostic exams, tumor morphology, cancer treatment, patients' comorbidities, performance and vital status was classified in three main categories of analysis:
 - Patient characteristics
 - Tumor factors
 - Healthcare determinants

Data source

- Data from Spanish cancer registration was complemented with information from patient's **clinical medical records**.
- Data were drawn following a detailed protocol from the European high-resolution studies collaboration **HIGHCARE project - Eranet TRANSCAN**: <http://www.hrstudies.eu/highcare.html>.
- Information regarding cancer stage at diagnosis (TNM, 7th Ed.), cancer diagnostic exams, tumor morphology, cancer treatment, patients' comorbidities, performance and vital status was classified in three main categories of analysis:
 - Patient characteristics
 - Tumor factors
 - Healthcare determinants

Methods: comorbidities/multi-morbidity

Methods: comorbidities

- All recorded comorbidities were extracted **six-months before** the index cancer case was diagnosed.
- Comorbidities were classified based on the **Royal College of Surgeons modified Charlson classification** [8]:

Myocardial infarction	Congestive heart failure
Peripheral vascular disease	Cerebrovascular disease
Dementia	Chronic pulmonary disease
Rheumatic disease	Liver disease
Diabetes mellitus	Hemiplegia/paraplegia
Renal disease	AIDS/HIV

[8] Brusselaers, N. and J. Lagergren, The Charlson Comorbidity Index in Registry-based Research. *Methods Inf Med.* 2017;56(5):401-406

multi-morbidity

Multi-morbidity was defined as the presence of **two or more** comorbidities.[6]

Methods: comorbidities/multi-morbidity

Methods: comorbidities

- All recorded comorbidities were extracted **six-months before** the index cancer case was diagnosed.
- Comorbidities were classified based on the **Royal College of Surgeons modified Charlson classification** [8]:

Myocardial infarction	Congestive heart failure
Peripheral vascular disease	Cerebrovascular disease
Dementia	Chronic pulmonary disease
Rheumatic disease	Liver disease
Diabetes mellitus	Hemiplegia/paraplegia
Renal disease	AIDS/HIV

[8] Brusselaers, N. and J. Lagergren, The Charlson Comorbidity Index in Registry-based Research. *Methods Inf Med.* 2017;56(5):401-406

multi-morbidity

Multi-morbidity was defined as the presence of **two or more** comorbidities.[6]

Statistical analysis

- **Prevalence** of each of the 12 different comorbidities for the cohort of CRC patients.

Statistical analysis

- **Prevalence** of each of the 12 different comorbidities for the cohort of CRC patients.
- **Frequency and distribution** of comorbidities by patient, tumor and healthcare factors using counts and proportions.

Statistical analysis

- **Prevalence** of each of the 12 different comorbidities for the cohort of CRC patients.
- **Frequency and distribution** of comorbidities by patient, tumor and healthcare factors using counts and proportions.
- **Comorbidity risk** (for each of the 12 comorbidities) by patient, tumor and healthcare factors using generalized linear models with binomial family and link log to derive **Prevalence ratios**.

Statistical analysis

- **Prevalence** of each of the 12 different comorbidities for the cohort of CRC patients.
- **Frequency and distribution** of comorbidities by patient, tumor and healthcare factors using counts and proportions.
- **Comorbidity risk** (for each of the 12 comorbidities) by patient, tumor and healthcare factors using generalized linear models with binomial family and link log to derive **Prevalence ratios**.

Visualization

- In order to reduce the high dimensionality of the data, we used **advanced visualization tools** helping to visualize and interpret the data: **radar-plots**, **heatmaps** and **forest plots** for the ten most common comorbidities.

Visualization

- In order to reduce the high dimensionality of the data, we used **advanced visualization tools** helping to visualize and interpret the data: **radar-plots**, **heatmaps** and **forest plots** for the ten most common comorbidities.
- **Open source web application:** watzilei.com/shiny/CoMCoR/

Visualization

- In order to reduce the high dimensionality of the data, we used **advanced visualization tools** helping to visualize and interpret the data: **radar-plots**, **heatmaps** and **forest plots** for the ten most common comorbidities.
- **Open source web application:** watzilei.com/shiny/CoMCoR/
- **Reproducibility:** GitHub repository:
(github.com/migariane/CoMCoR)

Visualization

- In order to reduce the high dimensionality of the data, we used **advanced visualization tools** helping to visualize and interpret the data: **radar-plots**, **heatmaps** and **forest plots** for the ten most common comorbidities.
- **Open source web application:** watzilei.com/shiny/CoMCoR/
- **Reproducibility:** GitHub repository:
(github.com/migariane/CoMCoR)

Results: pattern of comorbidities

Prevalence and Top Three

- More than half (**59%**) of colorectal cancer patients had one or more comorbidities six months before cancer diagnosis.

Results: pattern of comorbidities

Prevalence and Top Three

- More than half (**59%**) of colorectal cancer patients had one or more comorbidities six months before cancer diagnosis.
- The most common comorbidities were **diabetes** (23.6%), chronic obstructive pulmonary disease (**COPD**) (17.2%) and congestive heart failure (14.5%).

Results: pattern of comorbidities

Prevalence and Top Three

- More than half (**59%**) of colorectal cancer patients had one or more comorbidities six months before cancer diagnosis.
- The most common comorbidities were **diabetes** (23.6%), chronic obstructive pulmonary disease (**COPD**) (17.2%) and congestive heart failure (14.5%).

Results: pattern of comorbidities

Results by Sex and Age

- The pattern of comorbidities by sex shows a high prevalence of **COPD** among **male** (79%).

Results: pattern of comorbidities

Results by Sex and Age

- The pattern of comorbidities by sex shows a high prevalence of **COPD** among **male** (79%).
- 60% of patients with **dementia** or **rheumatologic** disease were **female**.

Results: pattern of comorbidities

Results by Sex and Age

- The pattern of comorbidities by sex shows a high prevalence of **COPD** among **male** (79%).
- 60% of patients with **dementia** or **rheumatologic** disease were **female**.
- **Dementia** was the most common comorbidity among **older** patients (75+ years), showing a higher proportion (30%) of late cancer diagnosis (**stage IV**), and the highest prevalence of **diagnosis at emergency room** (33%).

Results: pattern of comorbidities

Results by Sex and Age

- The pattern of comorbidities by sex shows a high prevalence of **COPD** among **male** (79%).
- 60% of patients with **dementia** or **rheumatologic** disease were **female**.
- **Dementia** was the most common comorbidity among **older** patients (75+ years), showing a higher proportion (30%) of late cancer diagnosis (**stage IV**), and the highest prevalence of **diagnosis at emergency room** (33%).

Web Application: Radar plot top 10 comorbidities

Pattern of comorbidities: radar plots

Comorbidities shown:

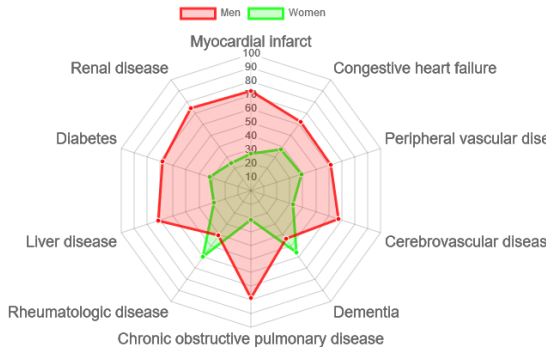
☒ Top 10
☐ Top 5

Comorbidities by:

Patient's characteristics ▼

☒ Sex
☐ Age
☐ Region
☐ Performance
☐ Smoking
☐ BMI

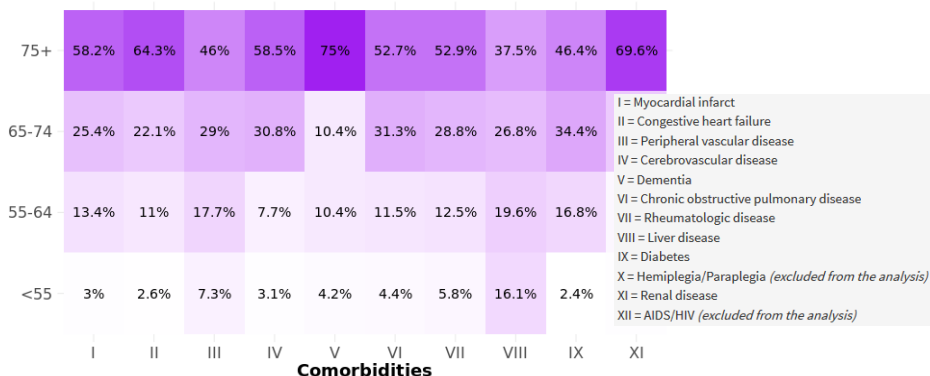
Percentage of patients having the comorbidity showing the characteristic selected



Open source web application: watzilei.com/shiny/CoMCoR/

Results: Web Application heat-map top 10 comorbidities

Percentage of patients having the comorbidity showing the characteristic selected

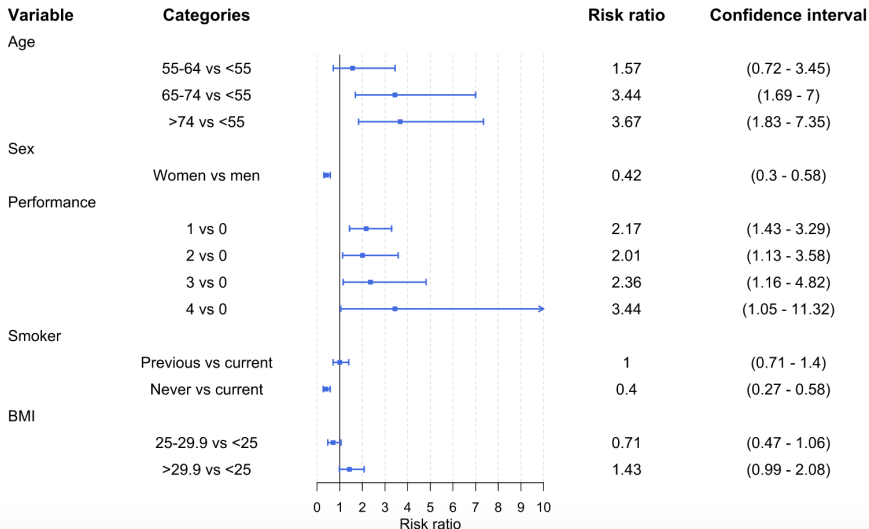


Open source web application:

watzilei.com/shiny/CoMCoR/

Web Application: Forest plot comorbidities' risk factors

Patient factors / Chronic pulmonary disease



Validity and Replicability

- **Generalizability** and **transportability** of results to other regions and countries.

Validity and Replicability

- **Generalizability** and **transportability** of results to other regions and countries.
- However, **similarities** with previous studies such as in the UK.

Validity and Replicability

- **Generalizability** and **transportability** of results to other regions and countries.
- However, **similarities** with previous studies such as in the UK.
- Replicability is the **strength** of the study.

Validity and Replicability

- **Generalizability** and **transportability** of results to other regions and countries.
- However, **similarities** with previous studies such as in the UK.
- Replicability is the **strength** of the study.
- Small size and just one calendar-year cohort.

Validity and Replicability

- **Generalizability** and **transportability** of results to other regions and countries.
- However, **similarities** with previous studies such as in the UK.
- Replicability is the **strength** of the study.
- Small size and just one calendar-year cohort.

Innovation and collaboration

- The assessment of cancer patients' comorbidities at a population-based level represents an **innovative** aspect of the study, as to date, such data are not available at a national level in Spain.

Innovation and collaboration

- The assessment of cancer patients' comorbidities at a population-based level represents an **innovative** aspect of the study, as to date, such data are not available at a national level in Spain.
- we are interested in **collaborative studies** (email us to discuss potential collaborations).

Innovation and collaboration

- The assessment of cancer patients' comorbidities at a population-based level represents an **innovative** aspect of the study, as to date, such data are not available at a national level in Spain.
- we are interested in **collaborative studies** (email us to discuss potential collaborations).
- Contact Details and Webpage: <http://comcor.netlify.com/>.

Innovation and collaboration

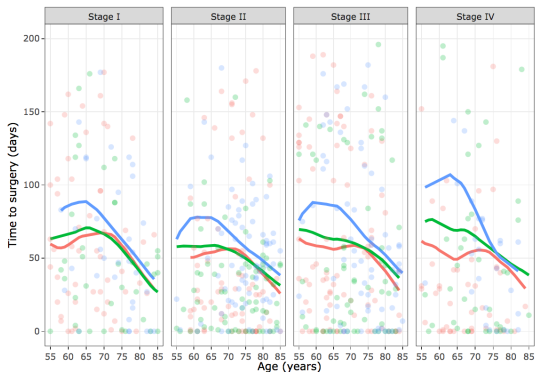
- The assessment of cancer patients' comorbidities at a population-based level represents an **innovative** aspect of the study, as to date, such data are not available at a national level in Spain.
- we are interested in **collaborative studies** (email us to discuss potential collaborations).
- Contact Details and Webpage: <http://comcor.netlify.com/>.
- **Next steps:** Impact of Comorbidities on the **Time** from Cancer Diagnosis to Surgery treatment.

Innovation and collaboration

- The assessment of cancer patients' comorbidities at a population-based level represents an **innovative** aspect of the study, as to date, such data are not available at a national level in Spain.
- we are interested in **collaborative studies** (email us to discuss potential collaborations).
- Contact Details and Webpage: <http://comcor.netlify.com/>.
- **Next steps:** Impact of Comorbidities on the **Time** from Cancer Diagnosis to Surgery treatment.

Next steps

- Time to surgery (non-parametric regression)



Number of comorbidities:

- No comorbidity
- One comorbidity
- Two or more

☐ Show heatmaps instead of tables

Stage I: Median of days (IQR)

	<55
No comorbidity	39(76)
One comorbidity	66(65)
Two or more comorbidities	41(247)

Stage II: Median of days (IQR)

	<55
No comorbidity	10(48)
One comorbidity	44(27)
Two or more comorbidities	0(0)

Stage III: Median of days (IQR)

	<55
No comorbidity	34(115)
One comorbidity	34(160)
Two or more comorbidities	59(269)

Stage IV: Median of days (IQR)

	<55
No comorbidity	20(72)
One comorbidity	96(202)
Two or more comorbidities	99(196)

Thank you!



Escuela Andaluza de Salud Pública
CONSEJERÍA DE SALUD



UNIÓN EUROPEA
Fondo Europeo de Desarrollo Regional

"Una manera de hacer Europa"

Miguel Ángel Luque-Fernández
miguel.luque.easp@juntadeandalucia.es
<https://maluque.netlify.com/>
<https://comcor.netlify.com/>

Carlos III Institute of Health, Grant/Award Number: **CP17/00206**
Andalusian Department of Health, Grant Number: **PI-0152/2017**