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 ($\geq 70$ years).[3]
Background

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]

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]
Background

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]
Background

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]


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.
Methods: Data

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.
Methods: Data

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:
Methods: Data

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
Methods: Data

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: Data

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]:

<table>
<thead>
<tr>
<th>Myocardial infarction</th>
<th>Congestive heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral vascular disease</td>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Dementia</td>
<td>Chronic pulmonary disease</td>
</tr>
<tr>
<td>Rheumatic disease</td>
<td>Liver disease</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Hemiplegia/paraplegia</td>
</tr>
<tr>
<td>Renal disease</td>
<td>AIDS/HIV</td>
</tr>
</tbody>
</table>


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]:

<table>
<thead>
<tr>
<th>Myocardial infarction</th>
<th>Congestive heart failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral vascular disease</td>
<td>Cerebrovascular disease</td>
</tr>
<tr>
<td>Dementia</td>
<td>Chronic pulmonary disease</td>
</tr>
<tr>
<td>Rheumatic disease</td>
<td>Liver disease</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Hemiplegia/paraplegia</td>
</tr>
<tr>
<td>Renal disease</td>
<td>AIDS/HIV</td>
</tr>
</tbody>
</table>


multi-morbidity

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

**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.
Methods: Statistical analysis

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**.
Methods: Statistical analysis

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**.
Methods: Data Visualization

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.
Methods: Data Visualization

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/
Methods: Data Visualization

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)
**Methods: Data Visualization**

**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/](watzilei.com/shiny/CoMCoR/)

- **Reproducibility:** GitHub repository: [github.com/migariane/CoMCoR](github.com/migariane/CoMCoR)
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

- Myocardial infarct
- Renal disease
- Congestive heart failure
- Peripheral vascular disease
- Cerebrovascular disease
- Diabetes
- Liver disease
- Rheumatologic disease
- Chronic obstructive pulmonary disease
- Dementia

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

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>75+</th>
<th>65-74</th>
<th>55-64</th>
<th>&lt;55</th>
</tr>
</thead>
<tbody>
<tr>
<td>I  = Myocardial infarct</td>
<td>58.2%</td>
<td>25.4%</td>
<td>13.4%</td>
<td>3%</td>
</tr>
<tr>
<td>II = Congestive heart failure</td>
<td>64.3%</td>
<td>22.1%</td>
<td>11%</td>
<td>2.6%</td>
</tr>
<tr>
<td>III = Peripheral vascular disease</td>
<td>46%</td>
<td>29%</td>
<td>17.7%</td>
<td>7.3%</td>
</tr>
<tr>
<td>IV = Cerebrovascular disease</td>
<td>58.5%</td>
<td>30.8%</td>
<td>7.7%</td>
<td>3.1%</td>
</tr>
<tr>
<td>V = Dementia</td>
<td>75%</td>
<td>10.4%</td>
<td>10.4%</td>
<td>4.2%</td>
</tr>
<tr>
<td>VI = Chronic obstructive pulmonary disease</td>
<td>52.7%</td>
<td>31.3%</td>
<td>11.5%</td>
<td>4.4%</td>
</tr>
<tr>
<td>VII = Rheumatologic disease</td>
<td>52.9%</td>
<td>28.8%</td>
<td>12.5%</td>
<td>5.8%</td>
</tr>
<tr>
<td>VIII = Liver disease</td>
<td>37.5%</td>
<td>26.8%</td>
<td>19.6%</td>
<td>16.1%</td>
</tr>
<tr>
<td>IX = Diabetes</td>
<td>46.4%</td>
<td>34.4%</td>
<td>16.8%</td>
<td>2.4%</td>
</tr>
<tr>
<td>X = Hemiplegia/Paraplegia (excluded from the analysis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XI = Renal disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>XII = AIDS/HIV (excluded from the analysis)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Open source web application:
watzilei.com/shiny/CoMCoR/
Web Application: Forest plot comorbidities’ risk factors

**Patient factors / Chronic pulmonary disease**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Categories</th>
<th>Risk ratio</th>
<th>Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55-64 vs &lt;55</td>
<td>1.57</td>
<td>(0.72 - 3.45)</td>
</tr>
<tr>
<td></td>
<td>65-74 vs &lt;55</td>
<td>3.44</td>
<td>(1.69 - 7)</td>
</tr>
<tr>
<td></td>
<td>&gt;74 vs &lt;55</td>
<td>3.67</td>
<td>(1.83 - 7.35)</td>
</tr>
<tr>
<td>Sex</td>
<td>Women vs men</td>
<td>0.42</td>
<td>(0.3 - 0.58)</td>
</tr>
<tr>
<td>Performance</td>
<td>1 vs 0</td>
<td>2.17</td>
<td>(1.43 - 3.29)</td>
</tr>
<tr>
<td></td>
<td>2 vs 0</td>
<td>2.01</td>
<td>(1.13 - 3.58)</td>
</tr>
<tr>
<td></td>
<td>3 vs 0</td>
<td>2.36</td>
<td>(1.16 - 4.82)</td>
</tr>
<tr>
<td></td>
<td>4 vs 0</td>
<td>3.44</td>
<td>(1.05 - 11.32)</td>
</tr>
<tr>
<td>Smoker</td>
<td>Previous vs current</td>
<td>1</td>
<td>(0.71 - 1.4)</td>
</tr>
<tr>
<td></td>
<td>Never vs current</td>
<td>0.4</td>
<td>(0.27 - 0.58)</td>
</tr>
<tr>
<td>BMI</td>
<td>25-29.9 vs &lt;25</td>
<td>0.71</td>
<td>(0.47 - 1.06)</td>
</tr>
<tr>
<td></td>
<td>&gt;29.9 vs &lt;25</td>
<td>1.43</td>
<td>(0.99 - 2.08)</td>
</tr>
</tbody>
</table>

Open source web application: watzilei.com/shiny/CoMCoR/
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.
Implications and further steps

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.
Implications and further steps

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).
Implications and further steps

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/](http://comcor.netlify.com/).
Implications and further steps

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/](http://comcor.netlify.com/).

Implications and further steps

**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/](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

**Stage I: Median of days (IQR)**
- No comorbidity: 39 (76)
- One comorbidity: 66 (65)
- Two or more comorbidities: 41 (247)

**Stage II: Median of days (IQR)**
- No comorbidity: 10 (48)
- One comorbidity: 44 (27)
- Two or more comorbidities: 0 (0)

**Stage III: Median of days (IQR)**
- No comorbidity: 34 (115)
- One comorbidity: 34 (160)
- Two or more comorbidities: 59 (269)

**Stage IV: Median of days (IQR)**
- No comorbidity: 20 (72)
- One comorbidity: 96 (202)
- Two or more comorbidities: 99 (196)
Thank you!

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