AIDM – Associazione Italiana Donne Medico Sez. di Reggio Emilia

COVID 19 e DIFFERENZE di GENERE:
dalla Epidemiologia ai Vaccini

Responsabile scientifico: *Maria Brini-Patologo Clinico*

Venerdì 28 maggio – ore 17,00 – 20,00

WEBINAR

Accreditamento ECM

Società Medica Lazzaro Spallanzani di Reggio Emilia

Provider ECM Nazionale standard n. 959

Con il patrocinio di:

Ordine dei Medici Chirurghi e degli Odontoiatri di Reggio Emilia

Diabete,Obesità e COVID in ottica di Genere

Valeria Manicardi

Specialista in Diabetologia

Coordinatore Annali Ass Medici Diabetologi

Ex Coordinatore Gruppo Donna – AMD

28 - maggio - 2021

Diabete, Obesità e Covid 19 in ottica di genere

- I fattori di rischio nella infezione da SARS-CoV2
- **Diabete :** i dati internazionali e i dati Italiani
  i dati della AUSL di Reggio E
- **Obesità :** i dati internazionali e i dati Italiani
  meccanismi fisiopatologici
- Conclusioni


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I fattori di rischio nella infezione da SARS-CoV2

PLOS

Research Article

Characteristics and outcomes of a cohort of COVID-19 patients in the Province of Reggio Emilia, Italy

Paolo Giorgi Rossi, Massimiliano Marino, Debora Formisano, Francesco Venturelli , Massimo Vicentini, Roberto Grilli, the Reggio Emilia COVID-19 Working Group

Published: August 27, 2020

Abstract

This is a population-based prospective cohort s
prevalence of COVID-19 and its prognostic fact
CoV-2 from February 27 to April 2, 2020 in the
cumulative incidence, hospitalization and deat
interval (95% CI) were calculated according to
higher prevalence of infection than males belo
20.86 ‰ over age 80). Case fatality rate reache
adjusting for age and comorbidities, men had a
of death (HR 1.6, 95% CI 1.2 to 2.1). Patients o
9.3) and HR 27.8 (95% CI 12.5 to 61.7) for hosp
risk of hospitalization (HR 1.3, 95% CI 0.99 to 1
hospitalization and of death were higher in pa
heart disease, diabetes, and hypertension, whi
1.4 to 2.5) but not of death (HR 1.1, 95% CI 0.7
of death (HR 0.97, 95% CI 0.69 to 1.34). Identif
considered when setting priorities in public health planning and clinical decision making.

	Hospitalization		Death	
	HR	95% CI	HR	95% CI
Sex				
Females	1		1	
Males	1.4	(1.2–1.6)	1.6	(1.2–2.1)
Age				
< 51	1		1	
51–60	1.3	(1.0–1.8)	1.5	(0.5–4.2)
61–70	3.2	(2.4–4.1)	3.8	(1.6–9.4)
71–80	5.9	(4.5–7.6)	9.1	(4.0–20.6)
≥ *81*	7.1	(5.4–9.3)	27.8	(12.5–61.7)
Calendar period				
before 15 March 2020	1		1	
from 16 to 22 March 2020	0.89	(0.74–1.01)	1.3	(0.9–1.8)
from 23 to 29 March 2020	0.91	(0.74–1.13)	0.5	(0.3–0.8)
Time from symptoms to diagnosis (days)				
OR per day	0.96	(0.94–0.97)	0.87	(0.84–0.90)
Place of birth				
Italy	1		1	
Abroad	1.3	(0.99–1.81)	1.03	(0.42–2.56)
Charlson Comorbidity Index				
0	1		1	
1	1.2	(0.93–1.5)	1.6	(1.0–2.5)
2	1.6	(1.2–2.0)	2.0	(1.3–3.1)
≥ 3	2.1	(1.6–2.6)	2.7	(1.9–3.9)

https://doi.org/10.1371/journal.pone.0238281.t004

2653 symptomatic patients tested positive for SARS-CoV2

February 27 to April 2, 2020 in the Reggio Emilia province

F: > rischio di infezione vs M sotto i 50 anni, ma < nelle età > 80
M > rischio di ospedalizzazione (HR:1,4) e di morte (1,6) vs F

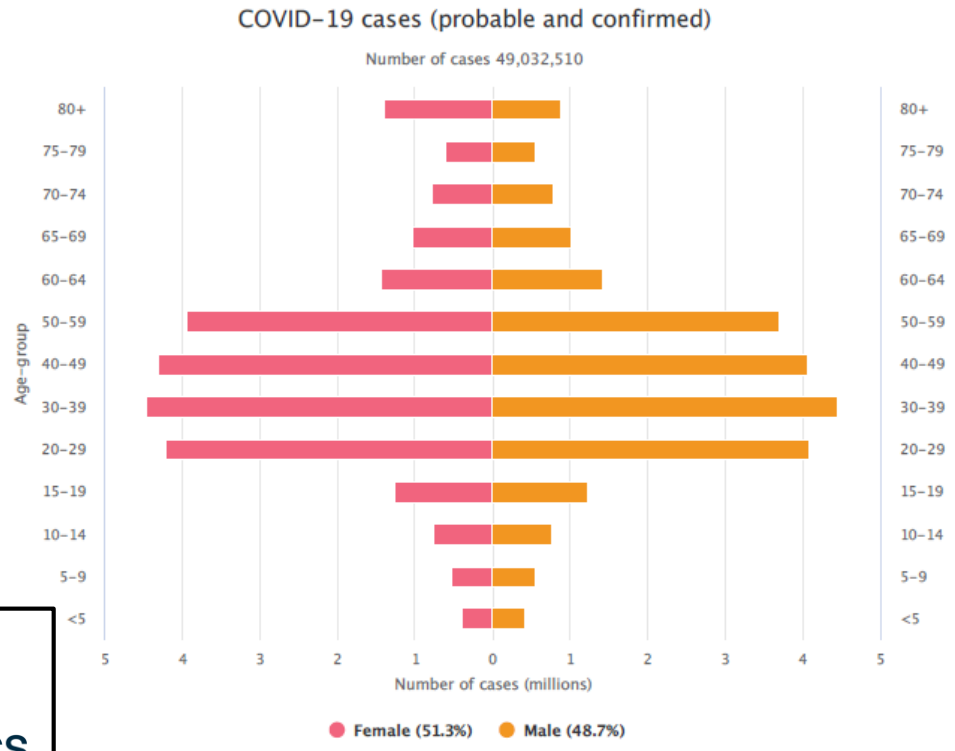
L'età > 80 anni ha un rischio di ospedalizzazione del 7,1 e di morte del 27,8 vs età < 50 a.

Fattori associati alla severità di malattia risultano:

- **Sc Cardiaco**
- **Aritmie**
- **Demenza**
- **CHD**
- **Diabete**
- **Ipertensione**
- **BPCO (solo ospedalizzazione)**

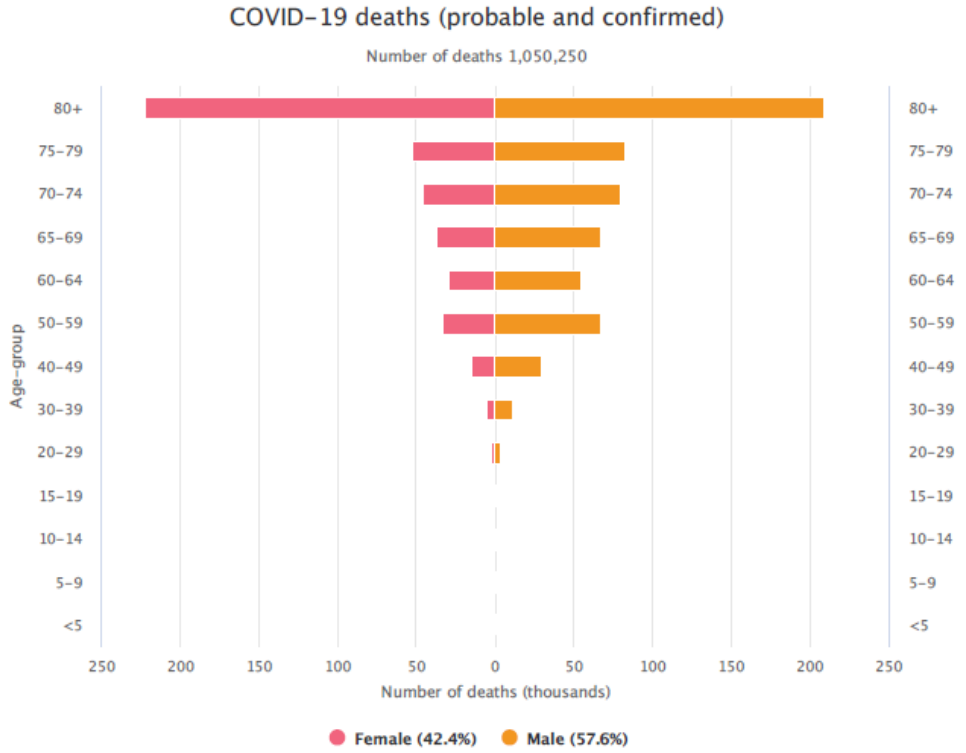
Covid 19 e Genere :

Mortalità: 3.2mln



-19) surveillance dashboard *(6)*.

of COVID-19 cases (probable and confirmed), by age and sex, January 2020 to April 2021



Source: WHO Coronavirus (COVID-19) surveillance dashboard *(6)*.

Fig. 1.5. Total number of COVID-19 deaths (probable and confirmed), by age and sex, January 2020 to April 2021

153mln nel mondo
Fine 2019 – 1 maggio 2021

Covid 19 e Genere : dati Italiani

ISS **: (20 aprile 2020)** la percentuale di **letalità** per gli uomini è circa il doppio di quella delle donne (17,1% e 9,3%)

- **L'età media** dei pazienti deceduti e positivi a SARS-CoV-2 è 81 a
- **età mediane**: pazienti con infezione 47 anni - pazienti deceduti 82 anni .
- **Le donne decedute sono il 43,9%.**
- **Le donne decedute** da SARS-CoV-2 hanno un'età più alta rispetto agli uomini (età mediana: **donne 86 anni – uomini 80 anni).**
- **maggior letalità per il genere maschile**: a fronte di un dato complessivo **del 5,7%,** la **letalità dei maschi è il 7,6% mentre quella delle femmine il 3,8%.**
- **l'*outcome* del COVID-19 acuto** è **più severo nel sesso maschile** ma le **reazioni autoimmuni** sono più frequenti nel **sesso femminile**.
- **Diabete e Obesità sono riconosciuti in molti studi sulla infezione da SARS-CoV 2 come fattori correlati ad ospedalizzazione, severità di malattia e morte**

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Diabete e Infezione da SARS-CoV2

Review

COVID-19 in people with diabetes: understanding the reasons for worse outcomes

Matteo Apicella*, Maria Cristina Campopiano*, Michele Mantuano*, Laura Mazoni*, Alberto Coppelli, Stefano Del Prato

Lancet Diabetes Endocrinol 2020; 8: 782–92

Published Online July 17, 2020 https://doi.org/10.1016/S2213-8587(20)30238-2

This online publication has been corrected. The corrected version first appeared at thelancet.com/diabetes-endocrinology on September 15, 2020 and further corrections on October 13.

Since the initial COVID-19 outbreak in China, much attention has focused on people with diabetes because of poor prognosis in those with the infection. Initial reports were mainly on people with type 2 diabetes, although recent surveys have shown that individuals with type 1 diabetes are also at risk of severe COVID-19. The reason for worse prognosis in people with diabetes is likely to be multifactorial, thus reflecting the syndromic nature of diabetes. Age, sex, ethnicity, comorbidities such as hypertension and cardiovascular disease, obesity, and a pro-inflammatory and pro-coagulative state all probably contribute to the risk of worse outcomes. Glucose-lowering agents and anti-viral treatments can modulate the risk, but limitations to their use and potential interactions with COVID-19 treatments should be carefully assessed. Finally, severe acute respiratory syndrome coronavirus 2 infection itself might represent a worsening factor for people with diabetes, as it can precipitate acute metabolic complications through direct negative effects on β-cell function. These effects on β-cell function might also cause diabetic ketoacidosis in individuals with diabetes, hyperglycaemia at hospital admission in individuals with unknown history of diabetes, and potentially new-onset diabetes.

Cause multifattoriali:

- Stato pro-infiammatorio
- Aumentato rischio infettivo
- Sistema immunitario meno efficiente
- Stato pro-trombotico (> PAI-1)
- Disfunzione endoteliale
- Comorbilità CV e renali e microvascolari
- Condizioni di scadente compenso metabolico

Segnalati casi di

- **Chetoacidosi** diabetica

- Ed **esordio improvviso Diabete T1 da distruzione B-Cellule**

Diabete e Covid 19: severità e mortalità

	Article type	Study population	Prevalence of diabetes	Outcome	Risk
Zhang et al[3]	Retrospective	258	24%	Mortality	3·64 (1·08–12·21)*
Kumar et al[4]	Meta-analysis	16 003	9·8%	Severe disease	2·75 (2·09–3·62)*
Kumar et al[4]	Meta-analysis	16 003	9·8%	Mortality	1·90 (1·37–2·64)*
Guan et al[10]	Retrospective	1590	NA	Composite†	1·59 (1·03–2·45)‡
Li et al[11]	Meta-analysis	1525	9·7%	ICU admission§	2·21 (0·88–5·57)¶
Fadini et al[12]	Meta-analysis	1687	NA	Severe disease	2·26 (0·98–4·82)‖
Fadini et al[12]	Meta-analysis	355	35·5%	Mortality	1·75‖
Petrilli et al[13]	Retrospective	5279	22·6%	Hospital admission	2·24 (1·84–2·73)*
Roncon et al[14]	Meta-analysis	1382	NA	ICU admission	2·79 (1·85–4·22)*
Roncon et al[14]	Meta-analysis	471	NA	Mortality	3·21 (1·82–5·64)*
Zhou et al[15]	Retrospective	191	19%	Mortality	2·85 (1·35–6·05)*
Zhu et al[16]	Retrospective	7337	13%	Mortality	1·49 (1·13–1·96)‡
Yan et al[17]	Retrospective	193	25%	Mortality	1·53 (1·02–2·3)‡
Sardu et al[18]	Retrospective	59	44%	Survival	0·172 (0·051–0·576)‡
Yang et al[19]	Meta-analysis	4648	NA	Severe disease	2·07 (0·88–4·82)*
Barron et al[20]	Cohort study	61 414 470	0·4% type 1 diabetes	Mortality	3·50 (3·15–3·89)*
Barron et al[20]	Cohort study	61 414 470	4·7% type 2 diabetes	Mortality	2·03 (1·97–2·09)*

ICU=intensive care unit. NA=not given. *Odds ratio (95% CI). †ICU admission, or invasive ventilation, or death. ‡Hazard ratio (95% CI). §Calculated for 1056 patients (in three of six studies). ¶Risk ratio (95% CI). ‖Rate ratio (95% CI not given).

Table 1: COVID-19 outcomes according to pre-existing diabetes

CORONADO Study non ha trovato una correlazione tra HbA1c e severità ed esito della infezione

Ma

Conferma la correlazione tra Glicemia all'ingresso ed esiti clinici

Review - Stefano Del Prato, Pisa

www.thelancet.com/diabetes-endocrinology Vol 8 September 2020

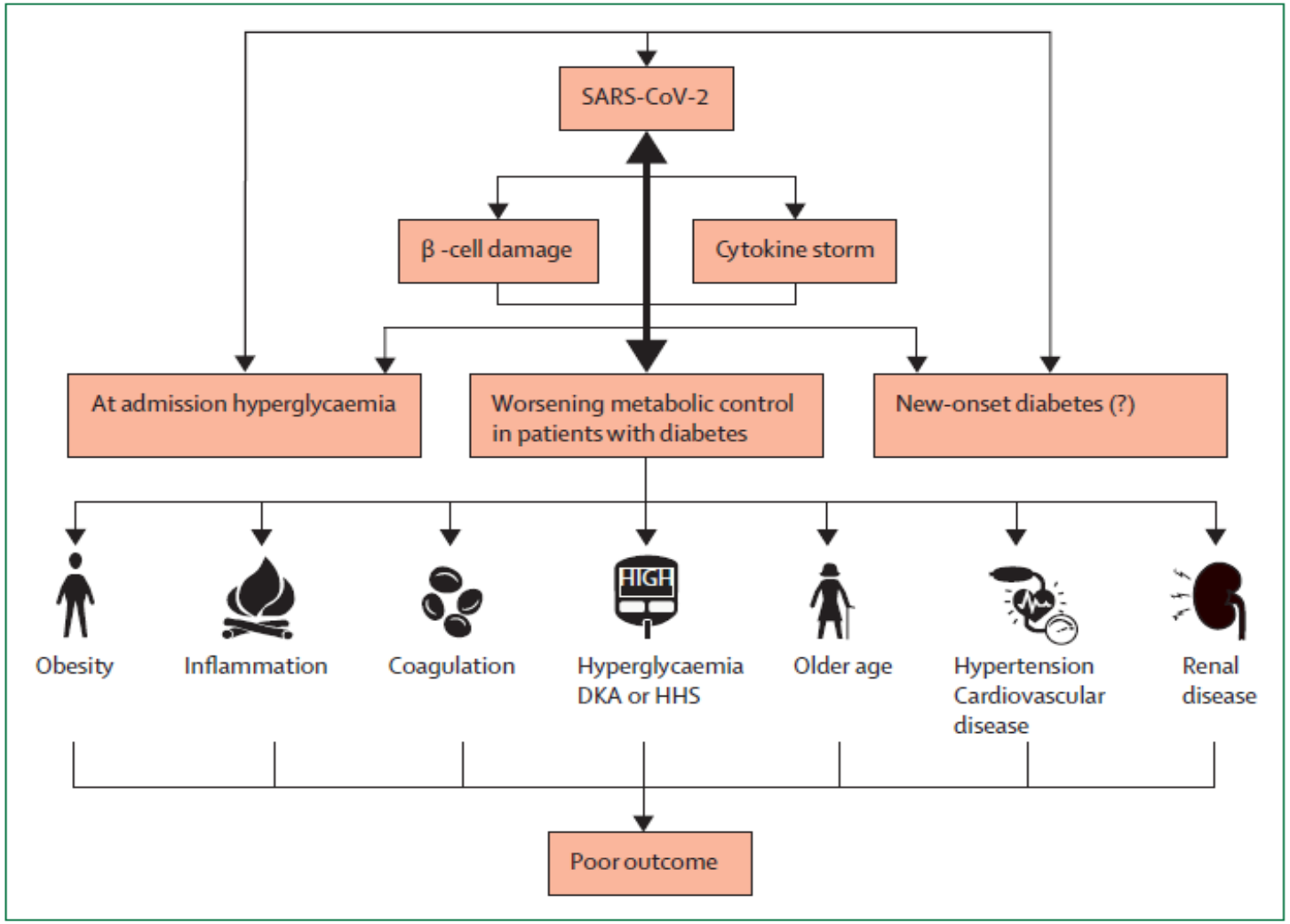


Figure: **Synopsis of the reciprocal effects of diabetes and COVID-19**
The relationship between diabetes and COVID-19 is biunivocal. On one hand, people with diabetes have worse outcomes because of multiple associated conditions enhancing the risk. On the other hand, SARS-CoV-2, because of its tropism for the β-cell, might cause new-onset diabetes or sustain hyperglycaemia at hospital admission. The impairment of β-cell function along with the inflammatory cytokine storm and counter-regulatory hormonal responses can precipitate further acute metabolic complications (DKA or HHS). New-onset diabetes, hyperglycaemia at admission, and acute metabolic deterioration, in turn, can further worsen COVID-19 outcomes. DKA=diabetic ketoacidosis. HHS=hyperglycaemic hyperosmolar syndrome.

Diabete e Covid 19

3 punti di attenzione per il Diabetico (sia T1 che T2) ricoveratp per COVID 19:

1. **Attento controllo metabolico dei valori glicemici con ter insulinica (anche per l'uso concomitante di Steroidi)**

2. **Attenzione alla possibile Ketoacidosi diabetica (controllo Ketoni e iperglicemia) e rischio Coma iperosmolare nell'anziano**

3. **Attenzione al possibile esordio di diabete ex novo**

Diabete e Covid 19

REVIEWS

Key points

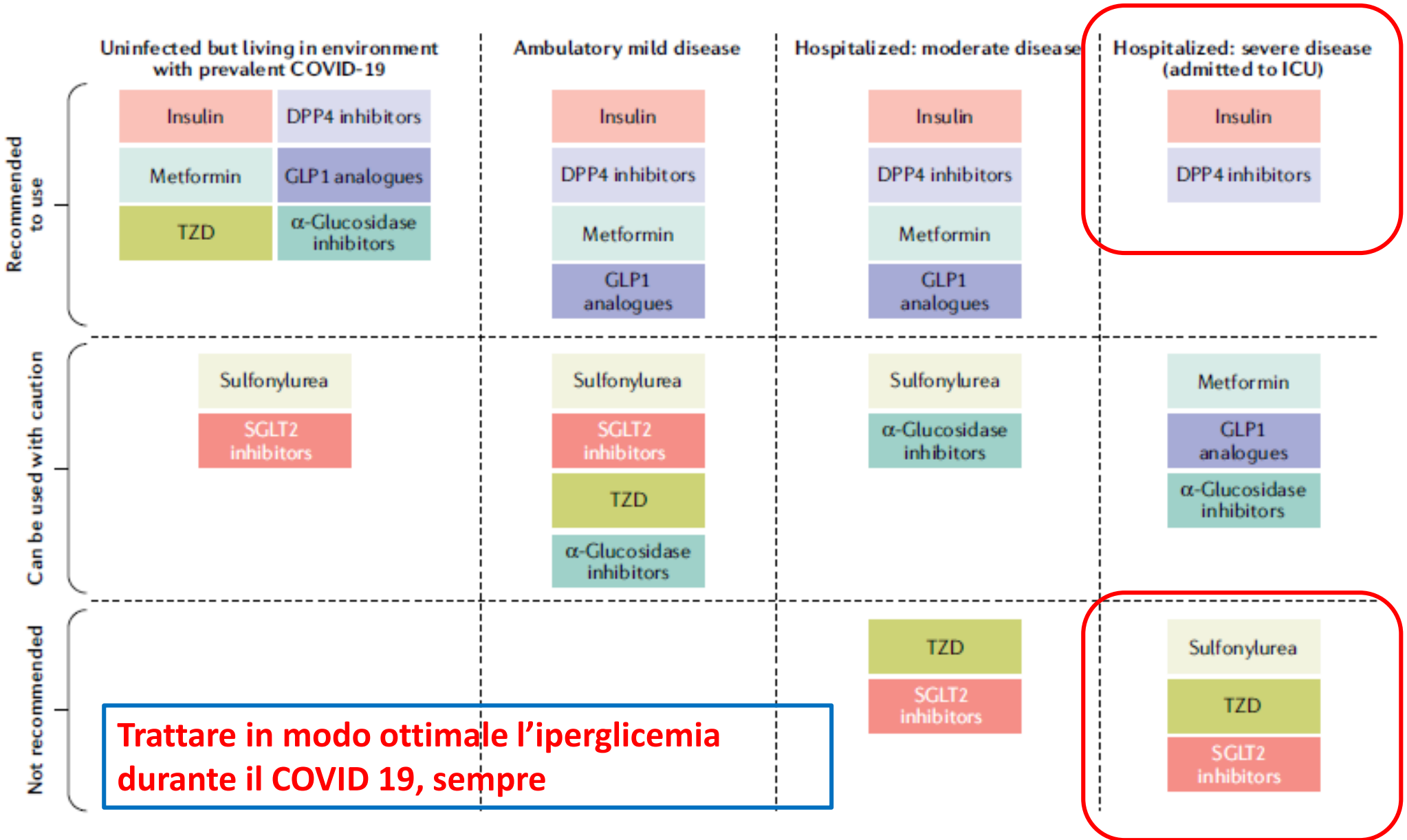
- Underlying diabetes mellitus and cardiovascular diseases are considered risk factors for increased coronavirus disease 2019 (COVID-19) disease severity and worse outcomes, including higher mortality.
- Potential pathogenetic links between COVID-19 and diabetes mellitus include effects on glucose homeostasis, inflammation, altered immune status and activation of the renin–angiotensin–aldosterone system (RAAS).
- During the COVID-19 pandemic, tight control of glucose levels and prevention of diabetes complications might be crucial in patients with diabetes mellitus to keep susceptibility low and to prevent severe courses of COVID-19.
- Evidence suggests that insulin and dipeptidyl peptidase 4 inhibitors can be used safely in patients with diabetes mellitus and COVID-19; metformin and sodium–glucose cotransporter 2 inhibitors might need to be withdrawn in patients at high risk of severe disease.
- Pharmacological agents under investigation for the treatment of COVID-19 can affect glucose metabolism, particularly in patients with diabetes mellitus; therefore, frequent blood glucose monitoring and personalized adjustment of medications are required.
- As COVID-19 lacks definitive treatment so far, patients with diabetes mellitus should follow general preventive rules strictly and monitor glucose levels more frequently, engage in physical activity, eat healthily and control other risk factors.

COVID-19 and diabetes mellitus: from pathophysiology to clinical management

Soo Lim[1,5]✉, *Jae Hyun Bae*[2,5], *Hyuk-Sang Kwon*[3] *and Michael A. Nauck*[4]✉

Abstract | Initial studies found increased severity of coronavirus disease 2019 (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in patients with diabetes mellitus. Furthermore, COVID-19 might also predispose infected individuals to hyperglycaemia. Interacting with other risk factors, hyperglycaemia might modulate immune and inflammatory responses, thus predisposing patients to severe COVID-19 and possible lethal outcomes. Angiotensin-converting enzyme 2 (ACE2), which is part of the renin–angiotensin–aldosterone system (RAAS), is the main entry receptor for SARS-CoV-2; although dipeptidyl peptidase 4 (DPP4) might also act as a binding target. Preliminary data, however, do not suggest a notable effect of glucose-lowering DPP4 inhibitors on SARS-CoV-2 susceptibility. Owing to their pharmacological characteristics, sodium–glucose cotransporter 2 (SGLT2) inhibitors might cause adverse effects in patients with COVID-19 and so cannot be recommended. Currently, insulin should be the main approach to the control of acute glycaemia. Most available evidence does not distinguish between the major types of diabetes mellitus and is related to type 2 diabetes mellitus owing to its high prevalence. However, some limited evidence is now available on type 1 diabetes mellitus and COVID-19. Most of these conclusions are preliminary, and further investigation of the optimal management in patients with diabetes mellitus is warranted.

Uso dei farmaci antidiabetici durante la infezione da COVID 19



SI

NO

Trattare in modo ottimale l'iperglicemia durante il COVID 19, sempre

Diabete e severità della Infezione da SARS-CoV2

Diabetologia
https://doi.org/10.1007/s00125-021-05458-8

ARTICLE

Risk phenotypes of diabetes and association with COVID-19 severity and death: a living systematic review and meta-analysis

Sabrina Schlesinger[1,2] · Manuela Neuenschwander[1,2] · Alexander Lang[1] · Kalliopi Pafili[2,3] · Oliver K[4] · Christian Herder[2,3,5] · Michael Roden[2,3,5]

Received: 9 December 2020 / Accepted: 17 March 2021

Abstract

Aims/hypothesis Diabetes has been identified as a risk factor for po…isease-2019 (COVID-19). The aim of this study is to identify high-risk phenotypes of diabet… severity and death.

Methods This is the first edition of a living systematic… observational studies investigating phenotypes in individuals with diabetes and COVID-… Four different databases were searched up to 10 October 2020. We used a random effects … mary relative risks (SRR) with 95% CI. The certainty of evidence was evaluated by the GR…

Results A total of 22 article…ais, met our inclusion criteria. For COVID-19-related death among individuals with diab… high to moderate certainty of evidence for associations (SRR [95% CI]) between male… studies), older age (>65 years: 3.49 [1.82, 6.69], $n=6$ studies), pre-existing comorbi… 1.56 [1.09, 2.24], $n=8$ studies; chronic kidney disease: 1.93 [1.28, 2.90], $n=6$ studies; ch… disease: 1.40 [1.21, 1.62], $n=5$ studies), diabetes treatment (insulin use: 1.75 [1.01, 3.03], $n=5$ …0.50 [0.28, 0.90], $n=4$ studies) and blood glucose at admission (≥11 mmol/l: 8.60 [2.25, 32.83], $n=2$ …out generally weaker and less precise associations were observed between risk phenotypes of diabetes and s… COVID-19.

Conclusions/interpretation Individuals with a more severe course of diabetes have a poorer prognosis of COVID-19 compared with individuals with a milder course of disease. To further strengthen the evidence, more studies on this topic that account for potential confounders are warranted.

Registration PROSPERO registration ID CRD42020193692.

Keywords COVID-19 · Diabetes · Meta-analysis · SARS-CoV-2 · Systematic review

TUTTI i DIABETICI SONO UGUALI ?

Meta-analisi, che ha incluso

- **22 studi** → totale di **17.687** p
- con diabete e infezione da Sars-CoV-2

Scopo : identificare i **fenotipi di diabete** ad alto rischio **associati alla gravità del Covid-19 e alla morte**

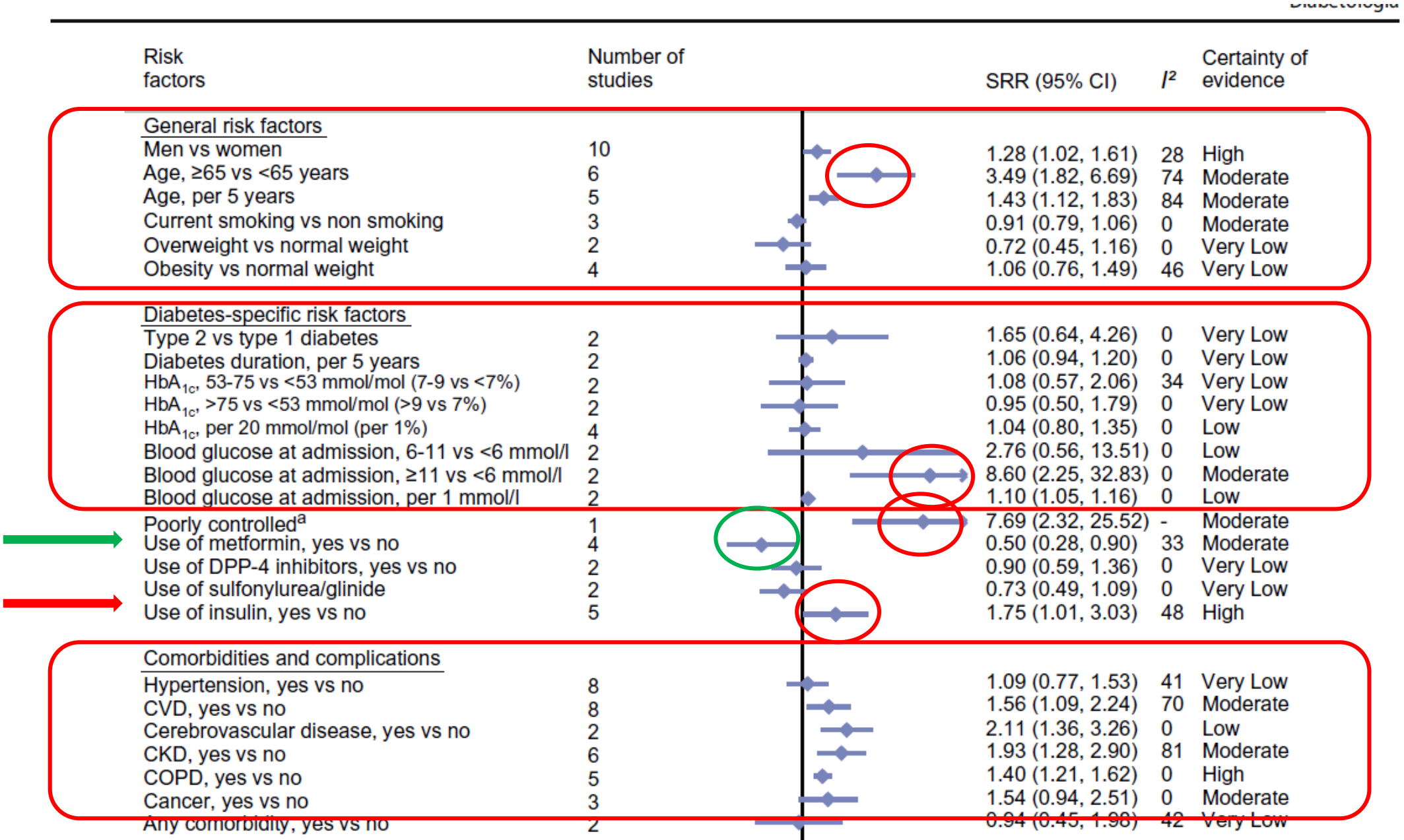
FdR per gravità e morte x Covid:

- **Sesso Maschile** > sesso Femminile
- **Età > 65 a.**
- **Complic CV e renali e BPCO**
- **Glicemia ingresso > 198 mg/dl**

Il tipo di trattamento :

- **Ter Insulinica cronica : peggiore outcome**
- Il trattamento cronico con **Metformina** si associa invece a un **rischio minore di decorso grave** della malattia → **protettiva ?**
- **(DPP4i ?)**

Diabete : Infezione da Covid 19 e mortalità



Risk factors	Number of studies	SRR (95% CI)	I^2	Certainty of evidence
General risk factors				
Men vs women	10	1.28 (1.02, 1.61)	28	High
Age, ≥65 vs <65 years	6	3.49 (1.82, 6.69)	74	Moderate
Age, per 5 years	5	1.43 (1.12, 1.83)	84	Moderate
Current smoking vs non smoking	3	0.91 (0.79, 1.06)	0	Moderate
Overweight vs normal weight	2	0.72 (0.45, 1.16)	0	Very Low
Obesity vs normal weight	4	1.06 (0.76, 1.49)	46	Very Low
Diabetes-specific risk factors				
Type 2 vs type 1 diabetes	2	1.65 (0.64, 4.26)	0	Very Low
Diabetes duration, per 5 years	2	1.06 (0.94, 1.20)	0	Very Low
HbA_{1c}, 53-75 vs <53 mmol/mol (7-9 vs <7%)	2	1.08 (0.57, 2.06)	34	Very Low
HbA_{1c}, >75 vs <53 mmol/mol (>9 vs 7%)	2	0.95 (0.50, 1.79)	0	Very Low
HbA_{1c}, per 20 mmol/mol (per 1%)	4	1.04 (0.80, 1.35)	0	Low
Blood glucose at admission, 6-11 vs <6 mmol/l	2	2.76 (0.56, 13.51)	0	Low
Blood glucose at admission, ≥11 vs <6 mmol/l	2	8.60 (2.25, 32.83)	0	Moderate
Blood glucose at admission, per 1 mmol/l	2	1.10 (1.05, 1.16)	0	Low
Poorly controlled[a]	1	7.69 (2.32, 25.52)	-	Moderate
Use of metformin, yes vs no	4	0.50 (0.28, 0.90)	33	Moderate
Use of DPP-4 inhibitors, yes vs no	2	0.90 (0.59, 1.36)	0	Very Low
Use of sulfonylurea/glinide	2	0.73 (0.49, 1.09)	0	Very Low
Use of insulin, yes vs no	5	1.75 (1.01, 3.03)	48	High
Comorbidities and complications				
Hypertension, yes vs no	8	1.09 (0.77, 1.53)	41	Very Low
CVD, yes vs no	8	1.56 (1.09, 2.24)	70	Moderate
Cerebrovascular disease, yes vs no	2	2.11 (1.36, 3.26)	0	Low
CKD, yes vs no	6	1.93 (1.28, 2.90)	81	Moderate
COPD, yes vs no	5	1.40 (1.21, 1.62)	0	High
Cancer, yes vs no	3	1.54 (0.94, 2.51)	0	Moderate
Any comorbidity, yes vs no	2	0.94 (0.45, 1.98)	42	Very Low

TUTTI i DIABETICI SONO UGUALI ?

- ✓ I **FdR** identificati quali **età, glicemia elevata, e complicanze possono identificare Diabetici più compromessi**
- ✓ Anche l'associazione con la **ter insulinica cronica identifica pazienti più compromessi (DT2 con complicanze Cv e renali severe)**
- ✓ **la METFORMINA** pazienti **Diabetici meno severi e in miglior controllo metabolico**

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WEBINAR

Registro Diabete a RE dal 2009

Prevalenza

DIABETES RESEARCH AND CLINICAL PRACTICE 103 (2014) 79–87

Contents available at ScienceDirect

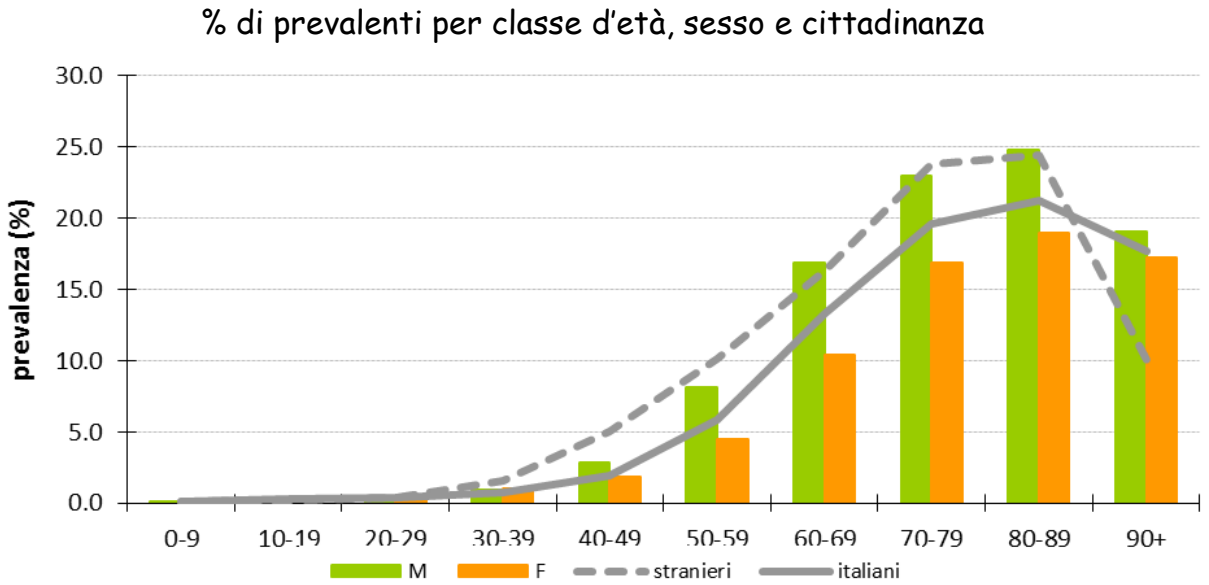
Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Building a population-based diabetes register: An Italian experience

Paola Ballotari[a], *Sofia Chiatamone Ranieri*[b,*], *Massimo Vicentini*[a], *Stefania Caroli*[a], *Andrea Gardini*[c], *Rossella Rodolfi*[d], *Roberto Crucco*[e], *Marina Greci*[f], *Valeria Manicardi*[g], *Paolo Giorgi Rossi*[a]



il **Link di 6 banche Dati**

tipo	N	%
DM2	29,588	90.4
DM1	1,164	3.6
Altro	269	0.8
ND	1,710	5.2
totale	32,731	100.0

Anno 2017

- **17924 (6,9%) maschi**
- **14807 (5,5%) femmine**
- **32731 (6,1%)** totale (intera provincia di Reggio Emilia)

Anno 2017

- 2583 (4%) stranieri
- 30148 (6,5%) italiani)

Diabete e Covid 19 a Reggio Emilia :

Link tra registro diabete e registro dati infezione da Sars-CoV2

Quesiti :

- Sono testati per Covid quanto la popolazione generale ?
- Sono più contagiati dal Covid rispetto alla Popolazione generale ?
- Hanno esiti peggiori ?
- Ci sono differenze di genere ?

Diabete e Covid_19 a Reggio Emilia

Table 1. Patients' pre-existing condition and clinical variables, by gender

	Female				Male			
Variables	**All Patients**	**Tested for the presence of SARS-CoV-2 n.(%)**	**Positive for the presence of SARS-CoV-2 n.(%)**	**Deaths n.(%)**	**All Patients**	**Tested for the presence of SARS-CoV-2 n.(%)**	**Positive for the presence of SARS-CoV-2 n.(%)**	**Deaths n.(%)**
N° (%)	273,535	8,598 (3.14)	2,540 (0.93)	256 (0.09)	265,797	6,690 (2.52)	1,988 (0.75)	276 (0.10)
Age, mean(sd)	46 (24.0)	57 (22.3)	62 (21.8)	86 (8.8)	43 (23.0)	56 (21.2)	60 (19.6)	80 (10.2)
NO Diabetes	260,134 (95.1)	7,818 (90.9)	2,271 (89.4)	202 (78.9)	249,253 (93.8)	5,833 (87.2)	1,683 (84.7)	201 (72.8)
Diab (Type1)	548 (0.2)	31 (0.4)	4 (0.2)	1 (0.4)	610 (0.2)	20 (0.3)	3 (0.2)	1 (0.4)
Diab (Type2)	11,896 (4.4)	689 (8.0)	243 (9.6)	49 (19.1)	15,017 (5.7)	786 (11.8)	291 (14.6)	73 (26.5)

Diabete e Covid_19 a Reggio Emilia

Table 2. Poisson regression models (adjusted for age), by gender

Variables	Female						Male					
	Tested for the presence of SARS-CoV-2		Positive for the presence of SARS-CoV-2		Deaths		Tested for the presence of SARS-CoV-2		Positive for the presence of SARS-CoV-2		Deaths	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
Diabetes (no)	1		1		1		1		1		1	
(Type1)	1.919	1.349-2.730	0.879	0.329-2.343	4.264	0.597-30.456	1.379	0.889-2.139	0.730	0.235-2.267	3.153	0.442-22.516
(Type2)	1.202	1.109-1.302	1.201	1.048-1.376	1.434	1.049-1.959	1.240	1.147-1.340	1.361	1.196-1.550	1.535	1.174-2.009
Charlson Comorbidity Index (0)									1			
(1)	2.007	1.840-2.190	1.812	1.558-2.107	2.272	1.634-3.159	1.628	1.477-1.795	1.453	1.225-1.722	2.269	1.642-3.135
(2)	1.712	1.557-1.881	1.632	1.385-1.922	2.962	2.089-4.201	2.034	1.845-2.241	1.613	1.349-1.928	2.696	1.928-3.772
(3)	2.710	2.417-3.038	2.062	1.661-2.560	3.704	2.089-4.201	3.090	2.774-3.443	1.993	1.607-2.472	3.074	2.086-4.530

Fattori di rischio nel Diabete per infezione e morte da covid 19

	Female						Male					
Variables	Tested for the presence of SARS-CoV-2		Positive for the presence of SARS-CoV-2		Deaths		Tested for the presence of SARS-CoV-2		Positive for the presence of SARS-CoV-2		Deaths	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
BMI (<25)	1		1		1		1		1		1	
(25-29.9)	0.853	0.628-1.158	0.759	0.413-1.394	**1.408**	0.423-4.683	0.924	0.730-1.169	**0.725**	0.474-1.109	**1.120**	0.430-2.917
(30-34.9)	1.196	0.883-1.618	**1.189**	0.660-2.145	**0.827**	0.184-3.723	0.910	0.701-1.181	**1.080**	0.699-1.668	**0.771**	0.235-2.533
(35-39.9)	1.117	0.763-1.635	**1.932**	1.019-3.665	**0.699**	0.077-6.307	1.178	0.842-1.648	**1.020**	0.554-1.878	**1.259**	0.252-6.289
(>39.9)	1.401	0.910-2.156	**1.497**	0.651-3.446	**4.704**	1.020-21.696	1.887	1.269-2.807	**2.748**	1.505-5.019	**4.311**	0.850-21.866
(missing)	1.718	1.334-2.212	**2.652**	1.649-4.267	**2.186**	0.771-6.198	1.187	0.949-1.485	**1.574**	1.081-2.291	**2.713**	1.156-6.371
Glicate_quart (<=7)	1		**1**		**1**		1		**1**		**1**	
(7-8)	0.868	0.718-1.050	**0.990**	0.723-1.356	**1.080**	0.508-2.293	0.960	0.810-1.137	**0.904**	0.679-1.203	**1.767**	1.041-3.000
(>8)	1.171	0.940-1.458	**1.201**	0.822-1.754	**2.397**	1.156- 4.972	1.043	0.848-1.282	**0.998**	0.705-1.412	**1.656**	0.834-3.287
(missing)	1.091	0.882-1.350	**1.293**	0.915-1.828	**1.510**	0.690-3.304	0.866	0.693-1.081	**1.019**	0.723-1.437	**0.840**	0.351-2.009
Durata diabete												
(<5)	1		**1**		**1**		1		**1**		**1**	
(5-15)	1.046	0.851-1.285	**1.243**	0.856-1.806	**1.162**	0.479-2.821	1.066	0.881-1.289	**1.170**	0.843-1.625	**5.201**	1.255-21.552
(>=15)	1.167	0.930-1.463	**1.405**	0.940-2.100	**1.359**	0.537-3.439	1.324	1.073-1.635	**1.655**	1.161-2.360	**6.241**	1.482-26.282

Comorbilità e Covid 19 _Diabetici F e M_ dati aggiustati per età

	Female						Male					
Variables	Tested for the presence of SARS-CoV-2		Positive for the presence of SARS-CoV-2		Deaths		Tested for the presence of SARS-CoV-2		Positive for the presence of SARS-CoV-2		Deaths	
	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI	IRR	95% CI
BPCO	2.227	1.669-2.973	**1.661**	0.967-2.852	**2.032**	0.730-5.660	2.320	1.831-2.940	**1.929**	1.267-2.937	**1.530**	0.663-3.532
Ischemic cardiopathy	1.493	1.162-1.918	**1.182**	0.748-1.868	**0.070**	0.240-2.474	1.494	1.249-1.787	**1.459**	1.083-1.965	**2.009**	1.189-3.395
Dementia	3.766	2.972-4.773	**5.038**	3.537-7.176	**5.328**	2.703-10.505	3.252	2.359-4.484	**3.953**	2.423-6.447	**2.329**	0.928-5.847
Chronic kidney failure	1.997	1.478-2.698	**1.245**	0.679-2.285	**1.377**	0.427-4.439	1.950	1.533-2.480	**1.001**	0.593-1.688	**1.858**	0.920-3.755
Cancer	1.094	0.868-1.380	**0.792**	0.507-1.238	**1.452**	0.654-3.225	1.413	1.185-1.685	**0.931**	0.668-1.298	**1.312**	0.752-2.289
Hypertension	1.708	1.444-2.020	**1.305**	0.969-1.756	**1.666**	0.914-3.036	1.814	1.560-2.110	**1.437**	1.106-1.866	**1.836**	1.133-2.975
Heart failure	2.018	1.634-2.492	**1.476**	1.006- 2.166	**2.216**	1.120-4.384	1.768	1.433- 2.183	**1.557**	1.083-2.238	**2.090**	1.172-3.728
Arrhythmias	1.849	1.483-2.306	**1.336**	0.891-2.003	**1.625**	0.758-3.485	1.852	1.523-2.252	**1.674**	1.199-2.336	**2.104**	1.212-3.651
Vascular diseases	2.188	1.576-3.038	**1.696**	0.925-3.108	**1.968**	0.611-6.334	1.772	1.353-2.322	**1.152**	0.673-1.972	**1.122**	0.409-3.078
Cerebrovascular disease	2.153	1.748-2.651	**1.920**	1.346-2.740	**1.589**	0.739-3.418	2.305	1.902- 2.793	**2.240**	1.627-3.084	**2.853**	1.664-4.891

Rischio di Infezione

Rischio di Morte

Rischio di Infezione

Rischio di Morte

Diabete, Obesità e Covid 19 in ottica di genere

- I fattori di rischio nella infezione da SARS-CoV2
- Diabete : i dati internazionali
  i dati Italiani
  i dati della AUSL di Reggio E
- **Obesità : i dati internazionali , italiani e locali**
  Meccanismi fisiopatologici

Conclusioni

Le misure dell'Obesità

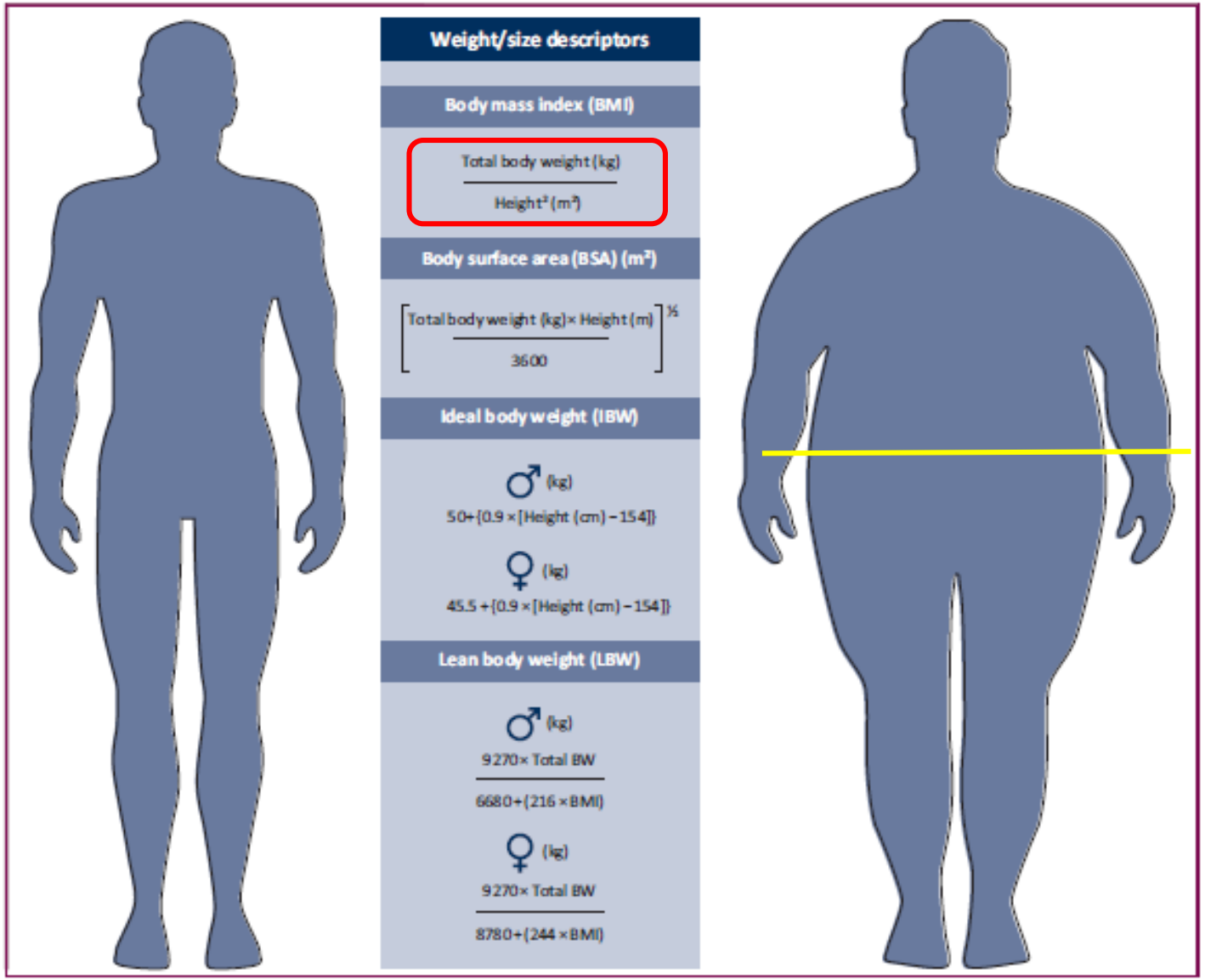


Figure 1. Summary of the most common weight and size descriptors and their limits.
Drug dose administration usually follows one of the three illustrated approaches: weight-based dosing, body-surface-area-based dosing, or fixed dosing. The first two strategies assume that drug PK parameters increase in proportion to increasing body size, whereas dosing drugs on a fixed basis presumes that body size does not influence drug PK parameters. Although commonly used to scale drug therapy in overweight or obese patients, each of these descriptors has important limitations. BMI and BSA are not informative as regards body composition and do not differentiate fat from lean tissue mass. IBW seems inappropriate as a dosing metric as it predicts the same dose for people of the same height, regardless of weight. LBW requires specialized equipment as it is measured with methods such as dual-energy X-ray absorptiometry, bioelectrical impedance analysis, underwater weighing and skinfold thickness.
BW, body-weight.

BMI: $\frac{\text{Peso KG}}{\text{Alt cm2}}$

Circonferenza vita:

F < 88 cm M < 102 cm

Diabetes and Overweight/Obesity Are Independent, Nonadditive Risk Factors for In-Hospital Severity of COVID-19: An International, Multicenter Retrospective Meta-analysis

https://doi.org/10.2337/dc20-2676

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*A complete list of International BMI-COVID consortium members is included in the supplementary material online.

This article is part of a special article collection available at https://care.diabetesjournals.org/collection/diabetes-and-COVID19.

OBJECTIVE

Obesity is an established risk factor for severe coronavirus disease 2019 (COVID-19), but the contribution of overweight and/or diabetes remains unclear. In a multicenter, international study, we investigated if overweight, obesity, and diabetes were independently associated with COVID-19 severity and whether the BMI-associated risk was increased among those with diabetes.

RESEARCH DESIGN AND METHODS

We retrospectively extracted data from health care records and regional databases of hospitalized adult patients with COVID-19 from 18 sites in 11 countries. We used standardized definitions and analyses to generate site-specific estimates, modeling the odds of each outcome (supplemental oxygen/noninvasive ventilatory support, invasive mechanical ventilatory support, and in-hospital mortality) by BMI category (reference, overweight, obese), adjusting for age, sex, and prespecified comorbidities. Subgroup analysis was performed on patients with preexisting diabetes. Site-specific estimates were combined in a meta-analysis.

RESULTS

Among 7,244 patients (65.6% overweight/obese), those with overweight were more likely to require oxygen/noninvasive ventilatory support (random effects adjusted odds ratio [aOR], 1.44; 95% CI 1.15–1.80) and invasive mechanical ventilatory support (aOR, 1.22; 95% CI 1.03–1.46). There was no association between overweight and in-hospital mortality (aOR, 0.88; 95% CI 0.74–1.04). Similar effects were observed in patients with obesity or diabetes. In the subgroup analysis, the aOR for any outcome was not additionally increased in those with diabetes and overweight or obesity.

CONCLUSIONS

In adults hospitalized with COVID-19, overweight, obesity, and diabetes were associated with increased odds of requiring respiratory support but were not associated with death. In patients with diabetes, the odds of severe COVID-19 were not increased above the BMI-associated risk.

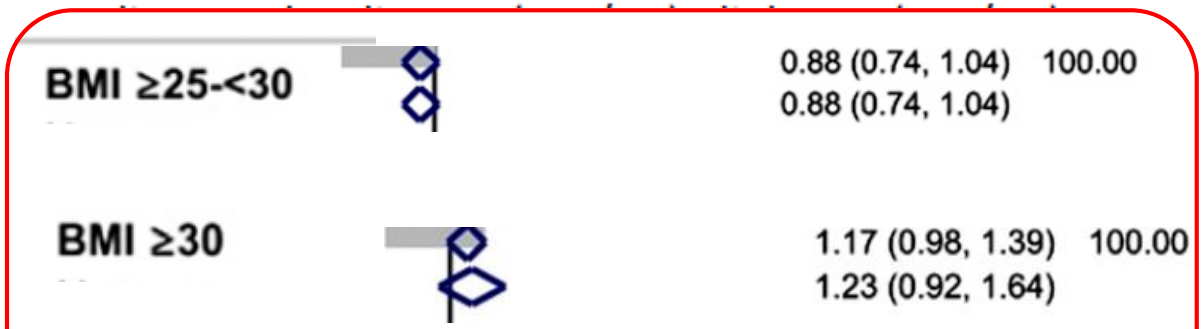
7,244 patients (65.6% overweight/obese)

hospitalized adult patients with COVID-19 from 18 sites in 11 countries.

60.1% M ; 39,9% F

Necessità di Ventilazione Meccanica

·Meta-analysis odds ratios for in-hospital mortality by BMI category.



BMI e Mortalità

Limiti dello studio: BMI < o > 30

Diabete : SI vs NO

Obesità : Classificazione

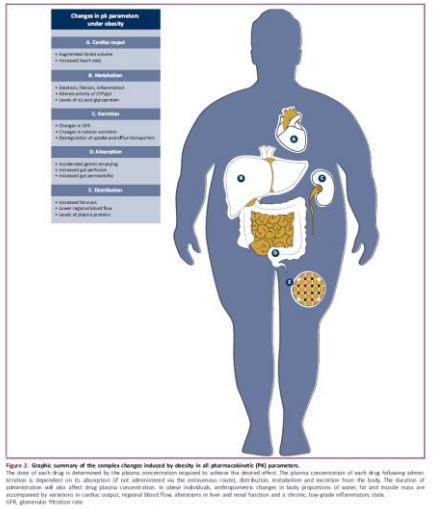
Table 1. BMI classification according to the World Health Organization (WHO)

WHO classification	BMI (kg/m^2)
Underweight	BMI $\leq$ 19.9
Normal weight	20 $\leq$ BMI $\leq$ 24.9
Overweight	25 $\leq$ BMI $\leq$ 29.9
Obesity grade I	30 $\leq$ BMI $\leq$ 34.9
Obesity grade II	35 $\leq$ BMI $\leq$ 39.9
Obesity grade III	BMI $\geq$ 40

BMI, body mass index; WHO, World Health Organization.

Rischio di forme severe di Covid 19 per BMI > 35 aumentato di 7 volte

OBESITA' VISCERALE



- **L' Obesità Viscerale** correla con il **rischio Cardio-Vascolare più del BMI**

…… ma anche con il rischio di maggiore severità della infezione da SARS-CoV2

e peggiore prognosi

Perché ? Ipotesi

- L'Obesità è caratterizzata da uno stato infiammatorio cronico……
- L'Obesità severa (BMI > 35) e soprattutto la grande obesità (BMI > 40) è caratterizzata da una insuff Respiratoria restrittiva
- L'Obesità severa è caratterizzata da uno stato procoagulativo.

Tutte condizioni che possono spiegare la maggiore severità della infezione da Covid 19 negli obesi

- cascata delle citochine

– Insuff respiratoria → necessità di Ventilazione Meccanica

- fenomeni trombotici diffusi (microvascolari)….

PLOS ONE

318 paz 27/2-13/3/2020

Composizione corporea alla TC toracica nei pazienti affetti da SARS-CoV2 e severità della malattia:

- la densità del ts muscolare è protettiva
- l'accumulo di grasso totale, ma soprattutto di Grasso Viscerale (VAT) correla con aumentato rischio di VM e/o Morte
- il Grasso Viscerale inoltre correla con alti livelli di PCR = > infiammazione
- la minore densità muscolare (anziani/obesi) correla con peggiore prognosi

RESEARCH ARTICLE

The impact of chest CT body composition parameters on clinical outcomes in COVID-19 patients

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Data Availability Statement: According to Italian law, anonymized data can only be made publicly

Abstract

We assessed the impact of chest CT
ease severity at hospital presentatio
mediation of body composition in the
Chest CT scans performed at hospita
27/2020-03/13/2020) were retrospec
total, visceral, and intermuscular adip
T8 vertebrae. Primary outcomes wer
death, death alone. Secondary outco
(SO2), CT disease extension at hosp
the effect of age on death was explor
age 65.7 years, females 37.7%), 205
and 58 (18.2%) died. Increased musc
TAT, VAT, and IMAT were risk factor
ters except TAT had borderline effec
SO2 and extension of lung parenchy
Approximately 3% of the effect of age
In conclusion, low muscle quality and
COVID-19 outcomes, VAT was asso
partly mediated the effect of age on n

Overall, our results confirm the association between adipose tissue, especially ectopic fat, and the inflammatory state driving disease severity and progression in COVID-19. VAT is known to be an endocrine organ with pro-inflammatory characteristics [13, 21] and different studies have measured higher levels of circulating inflammatory cytokines in people with visceral adiposity compared with lean individuals [13], leading to the hypothesis that they are susceptible to developing a more powerful cytokine storm during COVID-19 progression [41]. Moreover, abdominal obesity can profoundly alter pulmonary function by diminishing exercise capacity and augmenting airway resistance, resulting in increased respiratory fatigue [42]. Also, pectoral muscle density is a measure of respiratory muscle capacity, which is of central importance in COVID-19 patients undergoing MV. In fact, in these patients, death is frequently the consequence of muscle fatigue.

PlosOne - Besutti at all. – 2021 - Dati di Genere

Table 1. Clinical and body composition parameters in the population as a whole and in patients experiencing different outcomes.

Variables	All Patients	Hospitalization	Mechanical Ventilation	Death	Mechanical Ventilation or Dea
		N (%)	N (%)	N (%)	N (%)
	318	**205 (64.47)**	**68 (21.38)**	**58 (18.24)**	**97 (30.50)**
Age (years)	65.7 (52.8; 75.7)	71.8 (61.4; 79.8)	69.8 (63.2; 77.6)	79.8 (72.5; 85.0)	73.8 (66.4;82.5)
Females	120 (37.7)	69 (57.5)	16 (13.3)	13 (10.8)	27 (22.5)
Calendar period (Week 1)	36 (11.3)	27 (75.0)	15 (41.7)	8 (22.2)	17 (47.2)
(Week 2)	167 (52.5)	123 (73.7)	42 (25.2)	40 (24.0)	61 (36.5)
(Week 3)	115 (36.16)	55 (47.8)	11 (9.6)	10 (8.7)	19 (16.5)
Charlson Comorbidity Index (0)	239 (75.16)	134 (56.1)	45 (18.8)	27 (11.3)	58 (24.3)
(1)	22 (6.92)	18 (81.8)	7 (31.8)	7 (31.8)	11 (50.0)
(2)	20 (6.29)	18 (90.0)	6 (30.0)	5 (25.0)	8 (40.0)
(3)	37 (11.64)	35 (94.6)	10 (27.0)	19 (51.4)	20 (54.1)
Diabetes	43 (13.52)	41 (95.4)	20 (46.5)	11 (25.6)	23 (53.5)
COPD	10 (3.14)	10 (100)	3 (30.0)	7 (70.0)	9 (90.0)

Le **donne sono il 37,7%** dei pazienti con Covid 19 con accesso in PS (e metà sono ricoverate in osp: **69 F/136 M (205)**
Su **68** trattati **con VM solo 16 sono donne** e su **58 decessi solo 13 sono Donne**
I Diabetici sono **il 13 %** del totale**, il 20% dei ricoverati, il 29% dei paz ventilati, il 19% dei deceduti**

Obesità e Covid 19: Meccanismi fisiopatologici

Journal of Molecular Medicine
https://doi.org/10.1007/s00109-021-02072-4

JMolMed

REVIEW

Obesity and its impact on COVID-19

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Abstract

The severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) pandemic has proven a challenge to healthcare systems since its first appearance in late 2019. The global spread and devastating effects of coronavirus disease 2019 (COVID-19) on patients have resulted in countless studies on risk factors and disease progression. Overweight and obesity emerged as one of the major risk factors for developing severe COVID-19. Here we review the biology of coronavirus infections in relation to obesity. In particular, we review literature about the impact of adiposity-related systemic inflammation on the COVID-19 disease severity, involving cytokine, chemokine, leptin, and growth hormone signaling, and we discuss the involvement of hyperactivation of the renin-angiotensin-aldosterone system (RAAS). Due to the sheer number of publications on COVID-19, we cannot be completed, and therefore, we apologize for all the publications that we do not cite.

L'età spiega il 90 % della mortalità da infezione da SARS-CoV2

Il genere Maschile ha una mortalità **3 volte maggiore in fase acuta:**

- Elevati livelli di markers infiammatori , quali PCR e Ferritina
- Bassi livelli di recettori ACE2 antiinfiammatori
- Effetti del testosterone sulla proteasi Serina2 che interagisce con la Proteina Spike

Nel genere Femminile gli **Estrogeni** sembrano protettivi

-

Stato pro infiammatorio nell'obesità

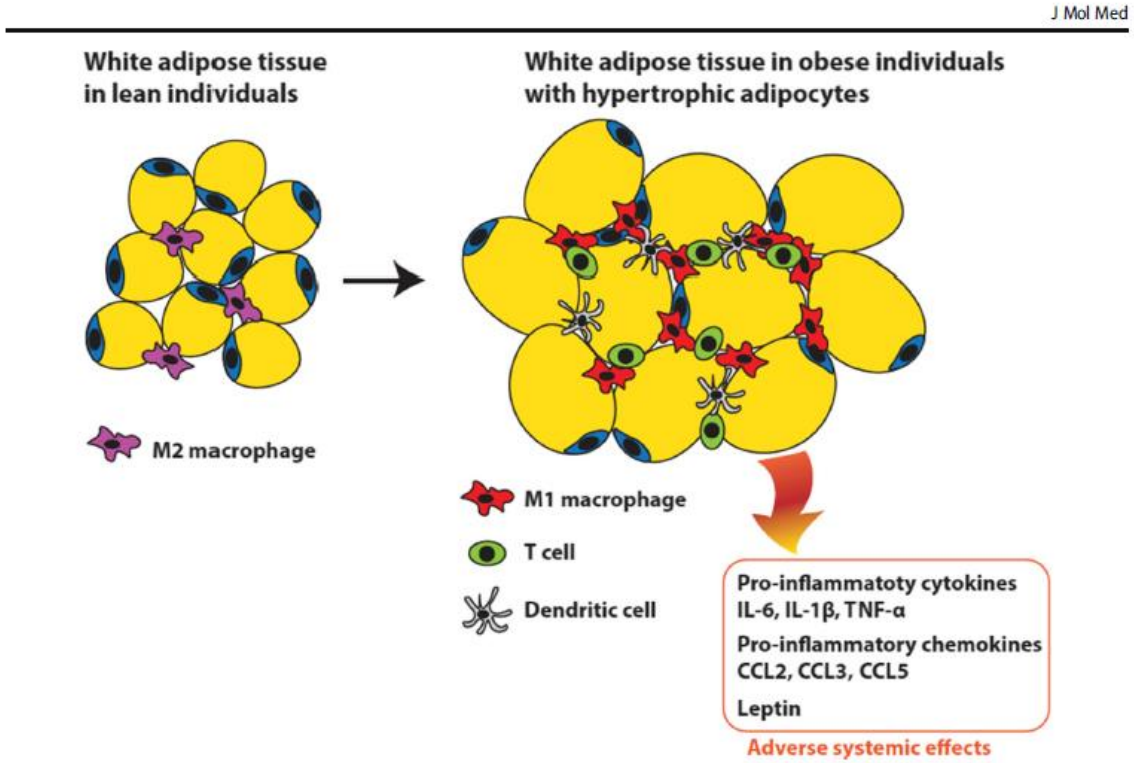

Fig. 2 Adverse systemic effects of fat accumulation in hypertrophic adipocytes. In obese individuals, a surplus of energy is stored as fat in hypertrophic adipocytes in the WAT. The hypertrophic fat cells secrete chemokines causing infiltration by immune cells and polarization of resident macrophages to the pro-inflammatory M1 type, resulting in elevated secretion of pro-inflammatory cytokines. In addition, high leptin secretion associated with leptin resistance in obese individuals further contributes to the inflammatory phenotype. Together, these processes elicit adverse systemic pro-inflammatory effects that aggravate COVID-19 symptoms. Figure based on Fig. 2 in [99]

L'obesità, dopo **l'età**, è il maggior fattore di rischio

- per **forme severe di Covid 19**,
- **per necessità di VM**
- per **aumentata mortalità**

solo nella

Ob severa (BMI >35) e soprattutto nella Grande Ob (BMI => 40)

- **Lo stato pro infiammatorio**
- **La maggiore facilità alle infezioni**
- **La Ridotta risposta immunitaria delle T-cell**
- **La ridotta espressione dei Recettori ACE2, ad az antiinfiammatoria**
- **Scarsa qualità della muscolatura toracica per infarcimento lipidico.**

Sono tra i possibili meccanismi fisiopatologici

Conclusioni 1

- **I Diabetici** non sembrano avere un maggior rischio di infezione da SARS-CoV2, ma se contagiati hanno un **decorso più severo, e maggiore mortalità soprattutto se:**

  - **maschi, di età> 65 anni, con scarso controllo metabolico e complicanze cardio vascolari e renali**

- **L'obesità** severa **(BMI>35)** è il secondo fattore di rischio di severità della malattia dopo l'età, e la **grande obesità (BMI > = 40)** correla con aumentato rischio di Morte, **sia nei M che nelle F**
- **Le donne,** sia **diabetiche che obese** hanno decorsi di malattia acuta meno severi e ridotta mortalità rispetto ai maschi.
- Nei **Maschi con D** la **durata di malattia, l'HbA1c e mal Cardio e Cer Vasc aumentano il rischio di Morte.**
- Nelle **Donne con D la durata di malattia non pesa sugli esiti, l'HbA1c SI**, come se la via fisiopatologica fosse diversa
- Il quadro è suggestivo di un maggior peso **nell'uomo** del **pathway di coagulazione**, mentre il **pathway infiammatorio** è importante per entrambi i sessi (vedi ruolo BMI) e forse soprattutto nelle donne
- la **parità di genere** potrebbe essere l'ennesima **vittima del Covid-19**

A commento del report ONU intitolato ***L'impatto del Covid-19 sulle donne***, uscito nell'aprile 2020, **António Guterres**, Segretario generale delle **Nazioni Unite**, afferma:

- ***I primi dati indicano che i tassi di mortalità da Covid-19 sembrano essere più alti per gli uomini, ma la pandemia sta avendo conseguenze sociali ed economiche devastanti per donne e ragazze.***

la **parità di genere** potrebbe essere l'ennesima **vittima del Covid-19.** Quasi cancellando le ultime conquiste sull'uguaglianza fra i sessi, la pandemia sembra riportare l'orologio indietro di cinquant'anni, arrestando la riduzione del ***gender pay gap*** e **ampliando il dislivello retributivo**.

Effetti collaterali del Covid 19

- **Il rapporto Global Gender Gap** del World Economic Forum per il **2020** classifica **l'Italia al 76° posto** su **153** paesi (in calo di sei posizioni rispetto al 2018).
- Durante i mesi di lockdown il **60% delle donne italiane** (contro **il 21%** degli uomini) si è trovato a dover gestire figli, famiglia e persone anziane, spesso insieme al lavoro

AIDM – Associazione Italiana Donne Medico Sez. di Reggio Emilia

COVID 19 e DIFFERENZE di GENERE:
dalla Epidemiologia ai Vaccini

Responsabile scientifico: *Maria Brini-Patologo Clinico*

Venerdì 28 maggio – ore 17,00 – 20,00

WEBINAR

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