



SC Cardiologia Polo Cardiologico - Ospedale di Cattinara

Attività di RICERCA

Centro di Riferimento per lo Scompenso Cardiaco e le Cardiomiopatie

La Struttura Complessa di Cardiologia dell'ASUGI di Trieste, rappresenta un riferimento nazionale ed internazionale per l'inquadramento, la gestione e la ricerca sulle Cardiomiopatie (CMP) e lo Scompenso Cardiaco (SC) con importanti collaborazioni cliniche e scientifiche con centri come ICGEB (International Centre for Genetic Engineering and Biotechnology), la Mayo Clinic di Rochester, MN, USA, il King's College London, UK, e l'Università di Denver, CO, USA, e con pubblicazioni su riviste peer-reviewed ad elevato Impact Factor (New England Journal of Medicine, Circulation, Journal of American College of Cardiology, European Heart Journal).

Semestralmente viene prodotto un aggiornamento del Registro sulle Cardiomiopatie. Ad oggi il Registro ha arruolato oltre 3000 pazienti di cui:

- 2000 con Cardiomiopatia Dilatativa/Cardiomiopatia Non Dilatata del Ventricolo sinistro,
- 5000 con Cardiomiopatia Ipertrofica,
- 120 con Cardiomiopatia Aritmogena del Ventricolo Destro,
- 220 con Miocardite biotpicamente accertate,
- 230 amiloidosi
- 100 altre forme di Cardiomiopatie,

risultando il registro monocentrico più numeroso al mondo sulla Cardiomiopatia Dilatativa completo di dati clinici al momento dell'esordio e durante il follow-up.

Presso la SC Cardiologia sono archiviati oltre 2000 campioni biologici condivisi tra la banca dati di Trieste e quella dell'Università di Denver, CO, USA.

Di questi campioni:

- 1300 appartengono a probandi affetti da diverse Cardiomiopatie.
- 750 campioni di probandi sono contenuti nell'archivio biologico nella sede di Trieste suddivisi per diverso tipo di Cardiomiopatia riscontrata.

Grazie alla Collaborazione con il Burlo Garofalo, ad oggi 657campioni sono stati analizzati mediante tecnologia di Panel Next Generation Sequencing ed hanno ottenuto un referto clinico certificato.

Nel campo dello SC, Cardiomiopatie e Miocarditi, viene offerta la possibilità di una completa caratterizzazione della patologia includendo anche metodiche avanzate, con protocolli specifici, come la Risonanza Magnetica Cardiaca, la Biopsia Endomiocardica e sua valutazione mediante caratterizzazione istopatologica, immunoistochimica e virologico molecolare, la caratterizzazione genetica mediante tecniche di Panel Next Generation Sequencing e lo studio e trattamento dei substrati aritmici mediante tecniche avanzate di mappaggio elettroanatomico ed ablazione radiofrequenza.

Oltre due terzi della casistica è gestita ambulatorialmente o in regime Day Hospital-Day Service.

Attività di Ricerca internazionale del Centro

Dal 1978 è stata sviluppata una attività strutturata di Registro e Ricerca nel campo dello Scompensamento Cardiaco e Cardiomiopatie. Tale attività è testimoniata dagli anni di prima pubblicazione dei contributi scientifici.

Ogni settimana si svolge un incontro di revisione ed aggiornamento sui casi ambulatoriali più controversi ed ogni mese si svolge un incontro di revisione critica e condivisione dei casi più complessi; semestralmente viene svolto un incontro di aggiornamento sullo stato di avanzamento dei progetti collaborativi, della ricerca e delle sottomissioni di lavori scientifici a riviste internazionali od a congressi internazionali.

La SC di Cardiologia collabora strettamente con l'IRCCS Burlo-Garofolo, con l'ICGEB e con la Faculty of Life Sciences & Medicine - King's College London, UK, per quanto riguarda gli aspetti di medicina traslazionale e rigenerativa. Tale collaborazione si è concretizzata a partire dal 2009 nella costituzione del Centro di Cardiologia Traslazionale, contiguo al Dipartimento Cardiovascolare con facilities di estrazione DNA, sequenziamento e laboratorio colture cellulari (Centro CTC, supportato da Assicurazioni Generali e Fondazione Cassa di Risparmio Trieste). Importanti studi di biologia molecolare sono stati condotti in collaborazione tra questi due centri al fine di migliorare la conoscenza dei meccanismi fisiopatologici alla base delle malattie cardiache e di identificare con sempre maggiore precisione ed efficacia possibili target terapeutici e modalità di diagnostica precoce e di miglioramento della sopravvivenza dei pazienti affetti da patologie cardiache.

E' intensamente attiva una collaborazione con l'Università di Denver CO, USA, e con la Mayo Clinic, Rochester, MN, USA, per la migliore definizione diagnostica e genetica delle Cardiomiopatie.

Appartenenza del Centro a network nazionali ed internazionali di Riferimento

LA SC di Cardiologia è interlocutrice e promotrice di accordi intra-regionali, nazionali, internazionali e transoceanici per la diagnosi e cura delle Cardiomiopatie e Scompensamento Cardiaco.

Attraverso lo strumento di partecipazione a reti collaborative (Fondazione Leduq [Trieste, London, Houston, Denver, Heidelberg, Utrecht, New York] ed accordi interuniversitari con Università di Denver CO, USA, CNR Pisa, Fondazione Monzino-MI, Stanford, CA, USA) il Centro promuove l'aggiornamento scientifico e gestisce Progetti di Ricerca anche mediante la partecipazione a Registri Internazionali.

Vengono coordinate dalla SC di Cardiologia le attività di partecipazione a registri e reti collaborative Internazionali quali:

- Rete ERN per le cardiomiopatie;
- Rete ERN per le cardiopatie rare;
- Share-ACM/DCM registry.

Collaborazioni di ricerca clinica con le seguenti Istituzioni:

- Policlinico di Milano (Carugo);
- Università degli studi di Genova e IRCCS san Martino (Canepa);
- Policlinico Sant'Orsola (Biagini);
- Fondazione Toscana Gabriele Monasterio (Edmin, Barison);
- Azienda Ospedaliera Universitaria Careggi (Olivotto, Fornaro);
- Azienda Ospedaliera Universitaria integrata Verona (Ribichini);
- ASST Grande Ospedale Metropolitano Niguarda (Ammirati);
- Policlinico di Bari (Guaricci);
- Azienda Ospedaliera Universitaria di Padova (Perazzolo Marra)
- Maastricht University Hopsital (Heymans)
- London – Imperial College (Prasad)
- Madrid (Garcia-Pavia)
- Mayo Clinic (Pereira)
- London – St. Thomas (Finocchiaro)
- King's College (McDonaugh-Cannatà)
- Richmond -VA (Abbate)
- John Hopkins (Adamo-Nilotra)

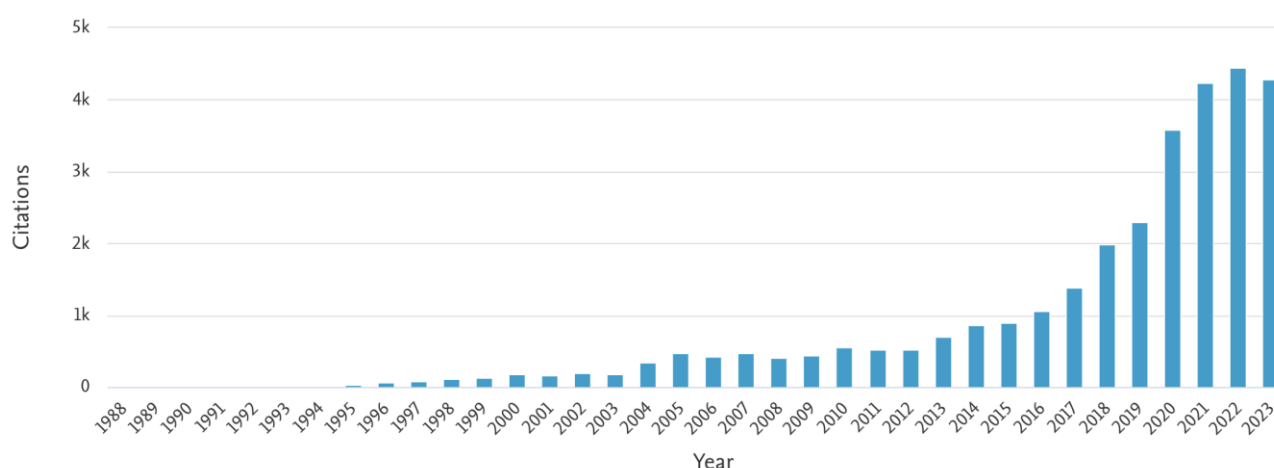
- Manchester (Nucifora)
- Milano - S. Raffaele (Peretto)
- Milano – S. Raffaele (Camici)
- NAC-London (Fontana-Gillmore)
- Padova (Perazzolo Marra)
- Pavia (Mazzanti)
- Messina (Di Bella)
- Roma (Autore)
- Rete di centri coinvolti nello studio della Amiloidosi
- Consorzio ARMADILLO (Amiloidosi)
- Brescia (Adamo, Metra, Tommasoni, Lombardi)
- John Hopkins (Gasperetti)
- Karolinska Institutet (Savarese, Lund, Manouras)
- MINICOR consortium (Gaztanaga)
- Hammersmith Hospital
- IPHNET rete italiana ipertensione polmonare
- Université libre de Bruxelles.
- Maastricht University Medical Centre, Maastricht,
- Ospedale di Novara
- Politecnico di Torino (D'ascenzio)
- University Hospital Leuven (Lesizza)
- ICGEB
- King's College Hospital
- IRCCS Humanitas
- Ospedale Burlo Garofolo

Attività Scientifica del Centro

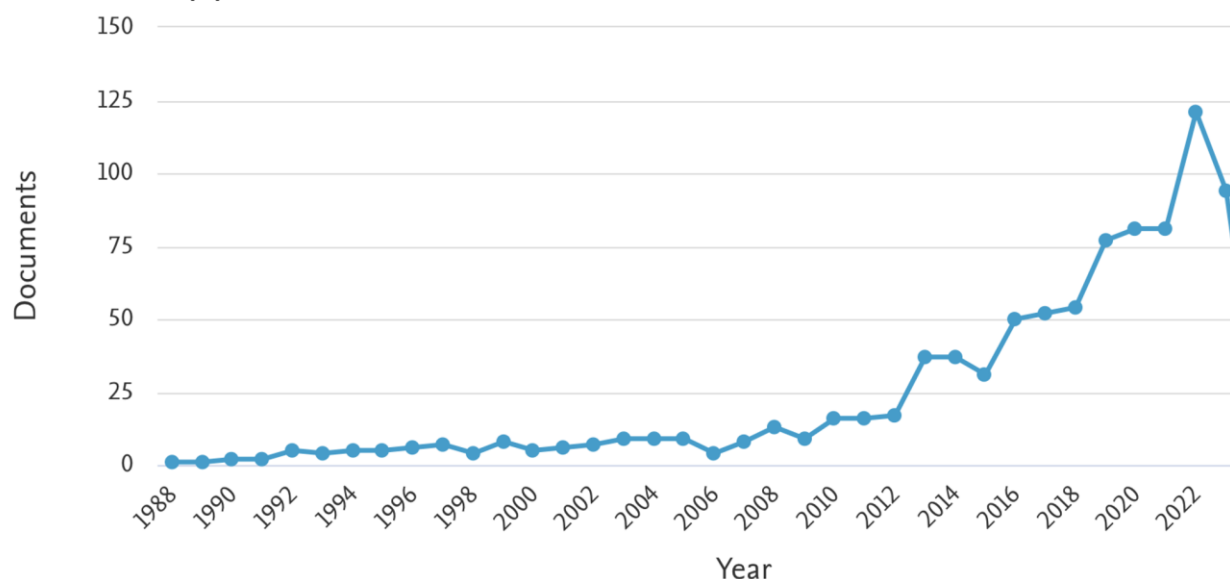
A partire dal 1988, l'attività scientifica conta oltre 650 pubblicazioni dei suoi professionisti su riviste internazionali e con un h-index di riferimento di 80 (dati Scopus/Web of Science). L'Impact Factor totale è di oltre 500 punti annui con numerose ricerche pubblicate su riviste internazionali prestigiose come Nature, New England Journal of Medicine, Circulation e J Am Coll Cardiol. Alcuni professionisti operanti presso la SC di Cardiologia di Trieste sono componenti di prestigiosi Editorial Board nazionali ed internazionali. Il dato di qualità dell'attività scientifica è sottolineato dal numero di citazioni dei lavori pubblicati. Negli ultimi anni sempre maggior attenzione viene posta dalla comunità scientifica ai lavori pubblicati con crescente aumento del numero di citazioni.

Di seguito un elenco selezionato di lavori pubblicati su riviste indicizzate medline **dal 2019 ad inizio 2024:**

Citations by year



Documents by year



1: Musumeci B, Tini G, Biagini E, Merlo M, Calore C, Ammirati E, Zampieri M, Russo D, Grilli G, Santolamazza C, Vio R, Rubino M, Ditaranto R, Del Franco A, Sormani P, Parisi V, Monda E, Francia P, Cipriani A, Limongelli G, Sinagra G, Olivotto I, Boni L, Autore C. Clinical characteristics and outcome of end stage hypertrophic cardiomyopathy: Role of age and heart failure phenotypes. *Int J Cardiol.* 2024 Apr 1;400:131784. doi: 10.1016/j.ijcard.2024.131784. Epub 2024 Jan 18. PMID: 38242504.

2: Andò G, Pelliccia F, Saia F, Tarantini G, Fraccaro C, D'Ascenzo F, Zimarino M, Di Marino M, Niccoli G, Porto I, Calabrò P, Gragnano F, De Rosa S, Piccolo R, Moscarella E, Fabris E, Montone RA, Spaccarotella C, Indolfi C, Sinagra G, Perrone Filardi P; Working Group of Interventional Cardiology of the Italian Society of Cardiology. Management of high and intermediate-high risk pulmonary embolism: A position paper of the Interventional Cardiology Working Group of the Italian Society of Cardiology. *Int J Cardiol.* 2024 Apr 1;400:131694. doi: 10.1016/j.ijcard.2023.131694. Epub 2023 Dec 30. PMID: 38160911.

3: Vatrano M, Manzi G, Picariello C, D'Alto M, Enea I, Ghio S, Caravita S, Argiento P, Garascia A, Vitulo P, Gabrielli D, Agostoni P, Corda M, Sinagra G, Grimaldi M, Scelsi L, Badagliacca R, D'Agostino C, Perrone Filardi P, Colivicchi F, Indolfi C, Roncon L, Galiè N, Oliva F, Vizza CD. Documento di consenso ANMCO/SIC sull'ipertensione arteriosa polmonare [ANMCO/SIC Consensus statement on pulmonary arterial hypertension]. *G Ital Cardiol (Rome).* 2024 Mar;25(3):192-201. Italian. doi: 10.1714/4209.42007. PMID: 38410902.

4: Pagnesi M, Riccardi M, Chiarito M, Stolfo D, Baldetti L, Lombardi CM, Colombo G, Inciardi RM, Tomasoni D, Loiacono F, Maccallini M, Villaschi A, Gasparini G, Montella M, Contessi S, Cocianni D, Perotto M, Barone G, Merlo M, Cappelletti AM, Sinagra G, Pini D, Metra M, Adamo M. Characteristics and outcomes of patients with tricuspid regurgitation and advanced heart failure. *J Cardiovasc Med (Hagerstown).* 2024 Mar 1;25(3):200-209. doi: 10.2459/JCM.0000000000001582. Epub 2024 Jan 9. PMID: 38251453.

5: Elia E, Bruno F, Crimi G, Wańha W, Leonardi S, Mauro M, Raposeiras Roubin S, Fabris E, Giannino G, Mancone M, Severino P, Truffa A, De Filippo O, Huczek Z, Mazurek M, Gaibazzi N, Ielasi A, Cortese B, Borin A, Núñez-Gil IJ, Marengo G, Melis D, Ugo F, Bianco M, Barbieri L, Marchini F, Desperak P, Morici N, Scaglione M, Gaşior M, Gallone G, Lopiano C, Stefanini G, Campo G, Wojakowski W, Abu-Assi E, Sinagra G, de Ferrari GM, Porto I, D'Ascenzo F. Gender differences in the development of heart failure after acute coronary syndrome: Insight from the CORALYS registry. *Int J Cardiol.* 2024 Feb 15;397:131622. doi: 10.1016/j.ijcard.2023.131622. Epub 2023 Dec 6. PMID: 38061607.

- 6: Botto GL, Sinagra G, Bulava A, Gargaro A, Timmel T, Giacobelli D, D'Onofrio A, Guédon-Moreau L. Predicting worsening heart failure hospitalizations in patients with implantable cardioverter defibrillators: is it all about alerts? A pooled analysis of nine trials. *Europace*. 2024 Feb 1;26(2):euae032. doi: 10.1093/europace/euae032. PMID: 38291778; PMCID: PMC10858640.
- 7: Pagnesi M, Sammartino AM, Chiarito M, Stolfo D, Baldetti L, Adamo M, Maggi G, Inciardi RM, Tomasoni D, Loiacono F, Maccallini M, Villaschi A, Gasparini G, Montella M, Contessi S, Cocianni D, Perotto M, Barone G, Merlo M, Cappelletti AM, Sinagra G, Pini D, Metra M, Lombardi CM. Clinical and prognostic implications of heart failure hospitalization in patients with advanced heart failure. *J Cardiovasc Med (Hagerstown)*. 2024 Feb 1;25(2):149-157. doi: 10.2459/JCM.0000000000001581. Epub 2023 Dec 22. PMID: 38149701.
- 8: Pagnesi M, Lombardi CM, Tedino C, Chiarito M, Stolfo D, Baldetti L, Adamo M, Cali F, Inciardi RM, Tomasoni D, Loiacono F, Maccallini M, Villaschi A, Gasparini G, Montella M, Contessi S, Cocianni D, Perotto M, Barone G, Merlo M, Cappelletti AM, Sinagra G, Pini D, Metra M. Role of ejection fraction in patients at risk for advanced heart failure: insights from the HELP-HF registry. *ESC Heart Fail*. 2024 Feb;11(1):136-146. doi: 10.1002/ehf2.14539. Epub 2023 Oct 16. PMID: 37845829; PMCID: PMC10804181.
- 9: Magri D, Gallo G, Piepoli M, Salvioni E, Mapelli M, Vignati C, Fiori E, Muthukkattil ML, Corrà U, Metra M, Paolillo S, Maruotti A, Di Loro PA, Senni M, Lagioia R, Scrutinio D, Emdin M, Passino C, Parati G, Sinagra G, Correale M, Badagliacca R, Sciomer S, Di Lenarda A, Agostoni P, Filardi PP. What about chronotropic incompetence in heart failure with mildly reduced ejection fraction? Clinical and prognostic implications from the Metabolic Exercise combined with Cardiac and Kidney Indexes score dataset. *Eur J Prev Cardiol*. 2024 Jan 25;31(2):263-271. doi: 10.1093/eurjpc/zwad338. Erratum in: *Eur J Prev Cardiol*. 2024 Jan 09;: PMID: 37890033.
- 10: Bertero E, Chiti C, Schiavo MA, Tini G, Costa P, Todiere G, Mabritto B, Dei LL, Giannattasio A, Mariani D, Lofiego C, Santolamazza C, Monda E, Quarta G, Barbisan D, Mandoli GE, Mapelli M, Sguazzotti M, Negri F, De Vecchi S, Ciabatti M, Tomasoni D, Mazzanti A, Marzo F, de Gregorio C, Raineri C, Vianello PF, Marchi A, Biagioni G, Insinna E, Parisi V, Ditaranto R, Barison A, Giammarresi A, De Ferrari GM, Priori S, Metra M, Pieroni M, Patti G, Imazio M, Perugini E, Agostoni P, Cameli M, Merlo M, Sinagra G, Senni M, Limongelli G, Ammirati E, Vagnarelli F, Crotti L, Badano L, Calore C, Gabrielli D, Re F, Musumeci G, Emdin M, Barbato E, Musumeci B, Autore C, Biagini E, Porto I, Olivotto I, Canepa M. Real-world candidacy to mavacamten in a contemporary hypertrophic obstructive cardiomyopathy population. *Eur J Heart Fail*. 2024 Jan;26(1):59-64. doi: 10.1002/ejhf.3120. Epub 2024 Jan 2. PMID: 38131253.
- 11: Merlo M, Setti M, Sinagra G. Coronary artery disease and dilated cardiomyopathy: Where parallel universes merge. *Eur J Heart Fail*. 2024 Jan;26(1):56-58. doi: 10.1002/ejhf.3095. Epub 2023 Dec 4. PMID: 37994286.
- 12: Zecchin M, Ciminello E, Mari V, Proclemer A, D'Onofrio A, Zanutto G, De Ponti R, Capovilla TM, Laricchiuta P, Biondi A, Sampaolo L, Pascucci S, Sinagra G, Boriani G, Carrani E, Torre M. A global analysis of implants and replacements of pacemakers and cardioverter-defibrillators before, during, and after the COVID-19 pandemic in Italy. *Intern Emerg Med*. 2024 Jan;19(1):107-114. doi: 10.1007/s11739-023-03450-1. Epub 2023 Nov 7. PMID: 37934343; PMCID: PMC10827813.
- 13: Aimo A, Milandri A, Barison A, Pezzato A, Morfino P, Vergaro G, Merlo M, Argirò A, Olivotto I, Emdin M, Finocchiaro G, Sinagra G, Elliott P, Rapezzi C. Electrocardiographic abnormalities in patients with cardiomyopathies. *Heart Fail Rev*. 2024 Jan;29(1):151-164. doi: 10.1007/s10741-023-10358-7. Epub 2023 Oct 17. PMID: 37848591; PMCID: PMC10904564.
- 14: Aimo A, Camerini L, Fabiani I, Morfino P, Panichella G, Barison A, Pucci A, Castiglione V, Vergaro G, Sinagra G, Emdin M. Valvular heart disease in patients with cardiac amyloidosis. *Heart Fail Rev*. 2024 Jan;29(1):65-77. doi: 10.1007/s10741-023-10350-1. Epub 2023 Sep 22. PMID: 37735319; PMCID: PMC10904406.

- 15: Fabris E, Boldrin C, Gregorio C, Pezzato A, Gagno G, Giannini F, Perkan A, Sinagra G. The Prognostic impact of treatments evolution in STEMI. *Int J Cardiol.* 2024 Jan 1;394:131352. doi: 10.1016/j.ijcard.2023.131352. Epub 2023 Sep 9. PMID: 37696362.
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- 17: Pezzato A, Fabris E, Gregorio C, Cittar M, Contessi S, Carriere C, Lardieri G, Zecchin M, Perkan A, Sinagra G. Implantable-cardioverter-defibrillator after ST-elevation myocardial infarction: when and how frequently is it implanted and what is the rate of appropriate interventions? Insight from Trieste registry. *J Cardiovasc Med (Hagerstown).* 2023 Dec 1;24(12):871-879. doi: 10.2459/JCM.0000000000001565. Epub 2023 Oct 16. PMID: 37851355.
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- 19: Nagyova E, Hoorntje ET, Te Rijdt WP, Bosman LP, Syrris P, Protonotarios A, Elliott PM, Tsatsopoulou A, Mestroni L, Taylor MRG, Sinagra G, Merlo M, Wada Y, Horie M, Mogensen J, Christensen AH, Gerull B, Song L, Yao Y, Fan S, Saguner AM, Duru F, Koskenvuo JW, Cruz Marino T, Tichnell C, Judge DP, Dooijes D, Lekanne Deprez RH, Basso C, Pilichou K, Bauce B, Wilde AAM, Charron P, Fressart V, van der Heijden JF, van den Berg MP, Asselbergs FW, James CA, Jongbloed JDH, Harakalova M, van Tintelen JP. A Systematic Analysis of the Clinical Outcome Associated with Multiple Reclassified Desmosomal Gene Variants in Arrhythmogenic Right Ventricular Cardiomyopathy Patients. *J Cardiovasc Transl Res.* 2023 Dec;16(6):1276-1286. doi: 10.1007/s12265-023-10403-8. Epub 2023 Jul 7. PMID: 37418234; PMCID: PMC10721666.
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- 23: Agostoni P, Pluchinotta FR, Salvioni E, Mapelli M, Galotta A, Bonomi A, Magri D, Perna E, Paolillo S, Corrà U, Raimondo R, Lagioia R, Badagliacca R, Perrone Filardi P, Apostolo A, Senni M, Iorio A, Correale M, Campodonico J, Palermo P, Cicoira M, Metra M, Guazzi M, Limongelli G, Contini M, Pezzuto B, Sinagra G, Parati G, Cattadori G, Carriere C, Cittar M, Matassini MV, Salzano A, Cittadini A, Masè M, Bandera F, Bussotti M, Mattavelli I, Re F, Vignati C, Lombardi C, Scardovi AB, Sciomer S, Passantino A, Emdin M, Di Lenarda A, Passino C, Santolamazza C, Moscucci F, Zaffalon D, Piepoli M; MECKI Score Research Group. Heart failure patients with improved ejection fraction: Insights from the MECKI score database. *Eur J Heart Fail.* 2023 Nov;25(11):1976-1984. doi: 10.1002/ejhf.3031. Epub 2023 Oct 3. PMID: 37702313.
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Attività Didattica e di Formazione

Il Centro è sede di formazione e tirocinio per numerosi Corsi di Laurea e Scuole di Specializzazione e Master ed in tali contesti viene sviluppata una intensa attività educativa e di formazione.

Vengono periodicamente organizzate e promosse le attività didattiche e di aggiornamento per gli operatori sanitari operanti in azienda ed operanti in altre aziende con la partecipazione di uditori e relatori anche internazionali.

Biennialmente, dal 1997, viene organizzato il Corso avanzato "Incontri in Cardiologia, Scapenso Cardiaco e Cardiomiopatie" che si svolge in due giornate, con lo scopo di confrontare esperienze e ricerche e di aggiornare i discenti sulle ultime acquisizioni ed esperienze nel campo. Il Corso ha come relatori professionisti provenienti da istituti nazionali ed internazionali ed attrae mediamente oltre 400 discenti anche da altre regioni d'Italia e da altri paesi d'Europa.

Il centro è anche promotore di congressi regionali organizzati con il supporto della SIC triveneto e di congressi internazionali tra i quali:

- Advances in Heart Failure, Cardiomyopathies And Pericardial Diseases organizzato con il supporto della Fondazione Menarini.

Annualmente vengono organizzati:

- incontri di aggiornamento in tema di management e imaging delle cardiomiopatie e scapenso cardiaco;
- attività di aggiornamento sulle Miocarditi e su problematiche di gestione clinica dei pazienti;

- corsi di Cardionursing, parallelamente ai Corsi “Incontri in Cardiologia”, per gli operatori sanitari (in particolare Infermieri) per l’aggiornamento sulla gestione dei casi complessi.

Complessivamente, vi è una attività annuale molto intensa (anche con eventi ECM) di confronto, revisione critica, meeting con oltre 700 incontri all’anno, calendarizzati, che coinvolgono gli specializzandi, il personale medico ed infermieristico e professionisti nazionali ed internazionali.

Attività di Scuola di Specializzazione Postlauream e di Didattica Universitaria

Il Centro è sede della Scuola di Specializzazione postlauream in Malattie dell’Apparato Cardiovascolare, è parte della rete del Dottorato in Biomedicina Molecolare e di Master di I e II livello in particolare in Emergenze e Urgenze. Conta 32 specializzandi operanti in tutte le sezioni del Centro ed in altre strutture ospedaliere della Regione Friuli Venezia Giulia ed Extra rete. Sono previsti periodi di formazione in strutture internazionali di riferimento per la diagnosi ed il trattamento delle patologie cardiovascolari, incluso lo Scompenso Cardiaco e le Cardiomiopatie. Alcune attività formative presso ICGEB ed il Laboratorio per la Cardiologia Traslazionale riguardano la Medicina Rigenerativa e Molecolare nel contesto dello Scompenso Cardiaco e la Genetica nel contesto delle Cardiomiopatie.

L’attività didattica per il Corso di Laurea in Medicina e Chirurgia, Biotecnologie, Scienze Infermieristiche, Scuole di Specializzazione, Dottorati e master dell’Università’ di Trieste, viene svolta anche con la collaborazione dei professionisti medici ed infermieri operanti nel Centro e nell’intera rete formativa (ICGEB, IRCCS Burlo, Centro Cardiovascolare, Azienda Santa Maria della Misericordia UD, Azienda S. Maria degli Angeli Pordenone, Aree di Emergenza FVG, Presidio Ospedaliero di Gorizia-Monfalcone).

La SC di Cardiologia è attiva nella promozione di scambi tra studenti e riceve annualmente studenti e professionisti provenienti da università nazionali ed estere che visitano o richiedono la frequenza nella struttura nell’ambito di vari programmi di cooperazione nazionale ed internazionale.