



Review Article

Cardiac cachexia in sub-Saharan Africa



Antonio Grimaldi^{a,b,c,*}, Annalisa De Concilio^{b,c}, Luca Marsero^{c,d}, Elvia Capritti^b,
Barbara Vergani^c, Maxwell Odida^a

^a St. Mary's Lacor Hospital, Gulu, Uganda

^b San Raffaele Scientific Institute, Università Vita-Salute, Milan, Italy

^c St Raphael of St Francis, Nsambya Hospital, Kampala, Uganda

^d San Luigi Gonzaga Hospital, University of Torino, Italy

ARTICLE INFO

Article history:

Received 14 March 2017

Accepted 23 August 2017

Available online 30 August 2017

Keywords:

Cachexia

Wasting syndrome

Heart failure

Rheumatic heart disease

ABSTRACT

Cachexia is a public health challenge around the Globe but data on prevalence rates in developing countries are very scarce. In sub-Saharan Africa wasting syndrome is mainly related to malaria, HIV infections, tuberculosis and end-stage heart disease and always associated with high-mortality and dismal quality of life regardless of age, urban or rural setting. We report two different cases affected by cardiac cachexia related to end-stage heart disease. The large age gap between patients highlights the current impact of medical services in Uganda ranging from low-resource rural settings to urban areas of the capital city under epidemiologic transition. The wasting syndrome occurring in both patients emphasizes as cachexia remains largely neglected and underestimated in most sub-Saharan African countries.

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1. Introduction

Malnutrition and cachexia represent a major health problem worldwide with over a billion persons, mostly women and children, suffering from hunger. Although more people every year die of hunger rather than AIDS, malaria, and tuberculosis combined, the wasting syndrome, which is assuming epidemic proportions in the developing countries, is frequently ignored. Cachexia (or wasting syndrome) is characterized by maladaptive responses, including anorexia and an increase in metabolic rate and is associated with low serum albumin, loss of body weight and muscle mass. Conversely, malnutrition, defined as a consequence

of inadequate or improper food, is characterized by adaptive responses, including hunger, preferential use of fat deposits for energy, and the maintenance of lean body mass. While malnutrition abnormalities can be reversed with food supplementation or diet modification, these approaches fail to treat cachectic patients. In Sub-Saharan Africa, where both conditions often coexist, patients with wasting syndrome usually come to consult doctors very late when surgical risks are prohibitive to ensure proper treatment.

2. Case report

A 7-year-old Acholi boy from Gulu – Northern Uganda – and a 82-year-old Muganda woman from Kampala – the capital city of Uganda – both presented with heart failure symptoms, decreased muscle strength and wasting syndrome. The clinical profile of the patients is shown in [Table 1](#). According to the low education level, it

* Corresponding author at: San Raffaele Hospital and Università Vita-Salute, Via Olgettina, 60, Milano, Italy.

E-mail address: grimaldi.antonio@hsr.it (A. Grimaldi).

Table 1
Clinical profile of patients.

	Patient 1	Patient 2
Age (years)	7	82
Gender	Male	Female
NYHA class	III–IV	IV
Main diagnosis	HF/RHD Severe MR	HF AS
Associated disease	Severe TR TB Malaria	Hypertensive cardiomyopathy HIV positive Type 2 diabetes
<i>Cachectic status</i>		
Lost body weight (kg)	7	13
Period of body weight loss (months)	8	9
Lost muscle mass – BMI/Z-score	BMI <16; –3 Z-score	BMI <23; urine creatinine appearance
<i>Laboratory parameters</i>		
HB (g/dl)	<12	<12
Values of Albumin (g/dl)	<3.2	<3.2
CRP (mg/l)	>10	>10
<i>Echocardiographic parameters</i>		
EDD (mm)	60	50
ESD (mm)	44	40
EDV (ml)	170	125
EF (%)	40	25
sPAP (mmHg)	70	60
RV systolic dysfunction	Mild	Moderate
Systemic venous congestion	Moderate	Severe
Pericardial effusion	Mild	Moderate
<i>Pharmacological treatment</i>		
	Diuretics/ace-inhibitors	Diuretics/ace-inhibitors Antidiabetics
<i>Response to calorie supplementation</i>		
		Oxygen therapy Not achieved

NYHA, New York Heart Association; HF, heart failure; RHD, rheumatic heart disease; MR, mitral regurgitation; TR, tricuspid regurgitation; AS, aortic stenosis; TB, tuberculosis; HIV, human immunodeficiency virus; BMI, body mass index; Hb, hemoglobin; CRP, C-reactive protein; EDD, end-diastolic diameter; ESD, end-systolic diameter; EDV, end-diastolic volume; ESV, end-systolic volume; EF, ejection fraction; sPAP, systolic pulmonary arterial pressure; RV, right ventricle.

was not possible to precisely define a detailed clinical history and all informations were provided by patient's next of kin. According to his mother's description, the little boy had progressively lost weight in the last 8 months becoming severely ill, despite sharing the same diet with his brothers. The old woman was a Mugandan farmer and was reported from her daughter to have been suffering from uncontrolled hypertension, type 2 diabetes and renal insufficiency. She was also HIV-positive and hardly able to undergo regular clinical follow-up. Both patients' diet was animal protein-deprived, consisting mainly of carbohydrates such as cassava, sweet potatoes and matoke.

On clinical examination their bodies appeared skinny along with atrophic limbs and very low fat-free mass index (Figs. 1 and 2). Blood pressure was 90/60 mmHg, the pulse 100 beats/min and a sustained apical beat was clearly visible on the left lateral chest (Supplementary Videos 1 and 2). At cardiac auscultation high-pitched pan-systolic mitral and tricuspid murmurs were clearly appreciated in the little boy and a harsh systolic murmur from calcified aortic stenosis and S3 gallop were audible in the lady.

Laboratory tests confirmed abnormal biochemistry, anemia (Hb < 12 g/L), low serum albumin (<3.2 g/L) and increased inflammatory markers. Chest radiograph showed severe cardiomegaly and pulmonary congestion (Fig. 1). Echocardiography revealed an advanced rheumatic heart disease with massive mitral and tricuspid regurgitation in the young patient (Fig. 3) and an end-stage cardiomyopathy from severe and untreated calcified aortic stenosis in the lady. Despite an appropriate treatment in intensive care unit, the old lady died during hospitalization for

multiorgan failure due to end-stage heart disease. The young patient was given a nutritional support program and, in spite of the prohibitive surgical risk, was scheduled for heart surgery. A monthly follow up was recommended, but he never returned to the clinic because he died for acute infective respiratory complications during follow up.

3. Discussion

Eradication of poverty and undernutrition is part of the Millennium Development Goals (MDGs) agreed upon by the United Nations Member States (<http://www.who.int/mediacentre/factsheets/fs290/en/>)¹.

Undernutrition is the underlying cause of death in 45% of all deaths among children under 5 years of age. Although the proportion of underweight children has declined from 28% to 17% between 1990 and 2013, there are still notable gaps in data. Countries in East, West and Southern Africa have made better progress than those in Central Africa.

Cachexia is a metabolic syndrome characterized by loss of body weight and muscle mass². Decreased skeletal muscle strength is considered a distinguishing clinical feature³ along with immunologic dysfunction from insufficient protein intake and energy delivery and impaired ability to maintain the integrity of protective barriers. A consensus statement recently proposed to diagnose cachexia for a unintentional weight loss exceeding 5% within the previous 6–12 months combined with specific symptoms (e.g. fatigue, anorexia), loss of muscle and biochemical abnormalities

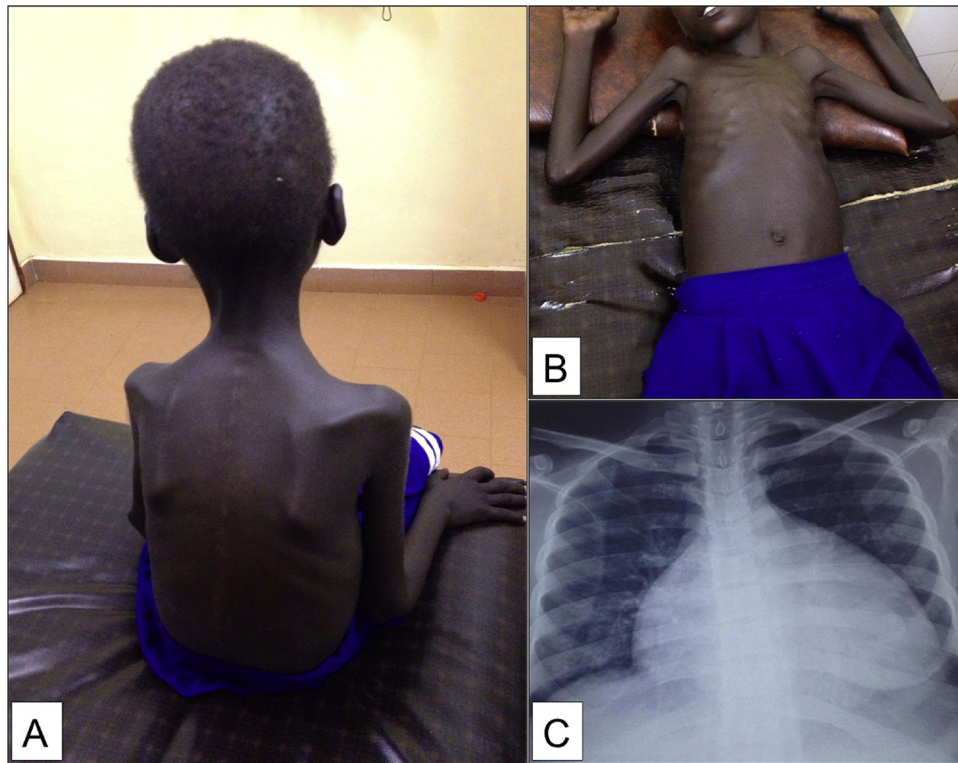


Fig. 1. (A) and (B) Cardiac cachexia in a young boy with severe rheumatic heart disease. (C) Chest X-ray showing severe cardiomegaly and pulmonary congestion due to massive mitral regurgitation.



Fig. 2. Cachectic state in a lady with end-stage cardiomyopathy due to calcified aortic stenosis.

such as anemia or inflammation. Loss of fat tissue is also thought to be a key-factor in the pathophysiology of cachexia even though fat, unlike muscle, cannot generate its own thermic energy.

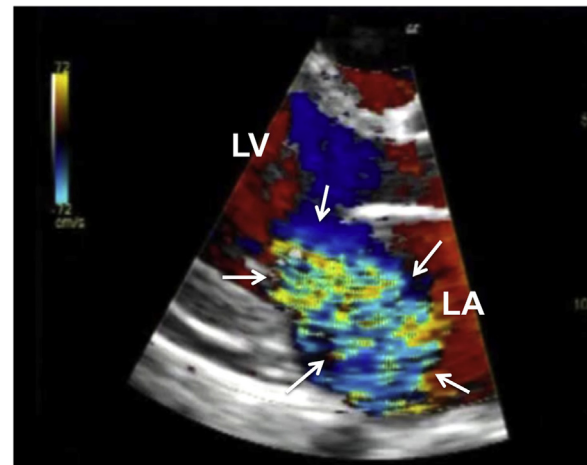


Fig. 3. Echocardiography. Parasternal long axis view showing severe rheumatic mitral regurgitation (arrows). LV, left ventricle; LA, left atrium.

In industrialized countries where the overall prevalence is growing approximately up to 1% (i.e., about nine million patients), cachexia develops in many chronic conditions including cancer, chronic heart failure (CHF), chronic obstructive pulmonary disease (COPD), chronic kidney disease, rheumatoid arthritis, stroke and infectious diseases such as HIV/AIDS, malaria, and tuberculosis^{4,5} (Table 2). Based on population prevalence, cachexia ranges from 5% to 15% in CHF or COPD to 60–80% in advanced cancer⁴. Cachexia has also been noted in patients after extensive traumatic injury and sepsis^{4,6}.

Mainly due to the lack of medical services, the data regarding the corresponding prevalence in the developing countries are scarce. In Africa, cachexia causes dramatic weight loss and

Table 2

Main causes of cachexia in developing and developed countries.

<i>Developing countries</i>	<ul style="list-style-type: none"> – Malaria – HIV/AIDS – Tuberculosis – Advanced heart disease (RHD, EMF, pericardial disease) – Undernutrition/malnutrition (suboptimal breastfeeding; deficiencies in micronutrients, iron, iodine, vitamin A, selenium and zinc; deficiencies in l-carnitine, thiamine and other B vitamins, aminoacids including taurine) – Poverty/starvation
<i>Developed countries and African settings under epidemiological transition</i>	<ul style="list-style-type: none"> – COPD – CHF (including malnutrition from mechanical cardiac support/heart transplantation in developed countries only) – Cancer (head and neck cancer, non-small cell lung cancer, pancreatic cancer and colorectal cancer) – CKD – Rheumatoid arthritis – HIV/AIDS – Stroke survivors – Nutritional complications associated with radiotherapy/chemotherapy – Aging/nursing home

RHD, rheumatic heart disease; EMF, endomyocardial fibrosis; COPD, chronic obstructive pulmonary disease; CHF, chronic heart failure; CKD, chronic kidney disease; AIDS, acquired immune deficiency syndrome.

muscular atrophy in several chronic illness including malaria, HIV infections, tuberculosis, cancer and advanced heart disease (i.e., rheumatic heart disease, endomyocardial fibrosis).

Patients generally come to medical attention at late stages of heart disease when surgical risks are prohibitive for proper treatment as in the cases reported. In patients with both tuberculosis and HIV co-infection, wasting may be also exacerbated⁷. Nutrition status and heart failure have strong associations in Africa where deficiencies in micronutrients, such as thiamine and selenium, for instance, are well known triggers of cardiomyopathy⁸. Malnutrition more commonly encountered in patients with advanced HF might progress to overt “cardiac cachexia,” which is characterized by protein-calorie malnutrition along with muscle wasting, enhanced inflammation and impaired homeostasis. Whilst the extreme state of the cases reported may be obvious, a less severe malnutrition can be challenging to recognize. Malabsorption with gut edema, limitations in eating and preparing food from fatigue, anorexia and increased work of breathing are all factors contributing to malnutrition in heart failure. The exact mechanism that causes cachexia is unknown but emerging evidence suggests that proinflammatory cytokines^{9,10} play a central role in the pathogenesis of cachexia. Cachexia is an adverse prognosticator in heart failure as it promotes persistent immune activation with high levels of inflammatory cytokines TNF, IL-1b, and IL-6 then enhancing the expression of various inflammatory mediators within the failing myocardium.

Currently, no specific treatment is available for cachectic patients. Whilst malnutrition is reversible when adequate amounts of food are provided, cachexia is not treatable by this approach. Death occurs when weight loss exceeds 30% and in starvation weight loss exceeding 40% of body weight is not compatible with life⁴. Treatment approaches using anabolics, anticatabolic therapies, orexigenic agents and nutritional interventions are under development^{4,9,10}.

The two cases also express the limited access to cardiac expertise and surgical programs that remain extremely limited in most sub-Saharan countries. Children living in many parts of Africa die in early teens or adulthood from the long-term effects of cardiac failure and related cachexia. Finally, in very low income settings, poverty, logistical difficulties (e.g. remoteness, lack of local healthcare resources) and/or cultural boundaries are all factors that may explain the difficulties in achieving adequate clinical follow up.

In conclusion, in Africa and around the Globe, body wasting is predominant in several chronic diseases, is highly predictive of increased mortality and contributes to the decline in quality of life that accompanies end-stage disease. Nutritional support alone may be inadequate in the management of cachexia. Treatments aimed at preventing and reversing cachexia are urgently needed to increase survival and to improve the quality of life for patients with chronic illnesses. The lack of medical services as well as public education/awareness are major obstacles to be overcome and constitute a public health challenge for this century.

Conflicts of interest

The authors have none to declare.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.ihj.2017.08.022>.

References

- English M, English R, English A. Millennium development goals progress: a perspective from sub-Saharan Africa. *Arch Dis Child*. 2015;100(suppl 1):S57–S58.
- Evans WJ, Morley JE, Argilés J, et al. Cachexia: a new definition. *Clin Nutr*. 2008;27:793–799.
- White JV, Guenter P, Jensen G, et al. Consensus statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *J Parenter Enteral Nutr*. 2012;36:275–283.
- von Haehling S, Anker SD. Cachexia as a major underestimated and unmet medical need: facts and numbers. *J Cachexia Sarcopenia Muscle*. 2010;1:1–5.
- Lainscak M, Filippatos GS, Gheorghide M, Fonarow GC, Anker SD. Cachexia: common, deadly, with an urgent need for precise definition and new therapies. *Am J Cardiol*. 2008;101:8–10.
- Farkas J, von Haehling S, Kalantar-Zadeh K, Morley JE, Anker SD, Lainscak M. Cachexia as a major public health problem: frequent, costly, and deadly. *J Cachexia Sarcopenia Muscle*. 2013;4:173–178.
- Lucas SB, De Cock KM, Hounnou A, et al. Contribution of tuberculosis to slim disease in Africa. *BMJ*. 1994;308:1531–1533.
- Soukoulis V, Dihu JB, Sole M, et al. Micronutrient deficiencies an unmet need in heart failure. *J Am Coll Cardiol*. 2009;54:1660–1673.
- Morley JE, Thomas DR, Wilson MM. Cachexia: pathophysiology and clinical relevance. *Am J Clin Nutr*. 2006;83:735–743 (Review).
- von Haehling S, Ebner N, Dos Santos MR, Springer J, Anker SD. Muscle wasting and cachexia in heart failure: mechanisms and therapies. *Nat Rev Cardiol*. 2017;14:323–341 (Review).